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VOLUME 238 APRIL 22, 1948 NUMBER 17

Carcinoma of the Stomach 583
Claude E. Welch and Arthur W. Allen

Complete Heart Block 589
Charles Fisch

Vaccination Against Influenza A and B . . . 593
R. I. Lienke, E. Perry Crump and John M. Adams

Acute Meningitis Caused by *Neisseria sicca* . . 596
Charlotte Bansmer and Jacob Brem

Medical Progress: Cancer 598
Grantley W. Taylor

Case Records of the Massachusetts General Hospital 602

Editorials:

British Medicine at the Crossroads 609
The Commonwealth Fund 610
Public Health — A Diagnosis 610
The Girls' Term 611

Obituary 612
Massachusetts Medical Society 613
Miscellany 613
Correspondence 613
Books Received 613
Notices 614

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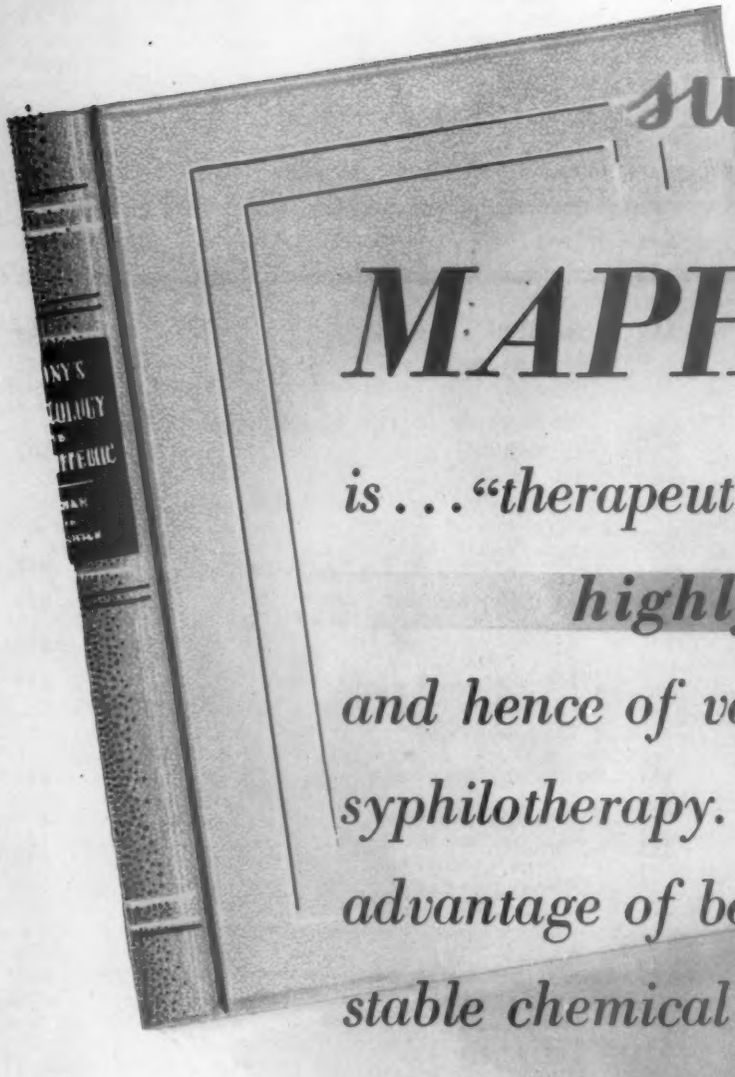

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*Cushny, A. R.: Pharmacology and Therapeutics, 13th Ed., Lea & Febiger, Philadelphia, 1947, p. 183.

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Volume 238 APRIL 22, 1948 Number 17

CARCINOMA OF THE STOMACH*

CLAUDE E. WELCH, M.D.,† AND ARTHUR W. ALLEN, M.D.‡

BOSTON

SURGICAL experience with carcinoma of the stomach at the Massachusetts General Hospital has been reviewed by Parsons[1] in previous papers covering the years 1922 to 1926, and the period from 1927 to 1936 by Parsons and Welch.[2] This report includes all patients admitted to this hospital on whom the diagnosis was made during the ten-year period 1937 to 1946 inclusive.

In the compilation of these figures, it is, of course, our hope to show that increased knowledge of the disease and its amenability to surgical attack have resulted in a steadily increasing five-year salvage rate. But it is of equal importance to consider the trends in management of patients with cancer of the stomach. In this brief summary, only our own experience can be considered, and no attempt is made to cover the voluminous literature comprehensively.

Several methods can be listed by means of which the curability rate can be increased. They are as follows: earlier diagnosis, that more patients with carcinoma will arrive in the hospital in a curable stage; more radical approach to the problem of gastric ulcer, that a certain number of cancers masquerading as ulcers will not be overlooked; extension of the type of operation so that by a wider excision of involved tissue, more cures may be obtained; and a reduction in the postoperative mortality, so that cases favorable for cure are not lost.

DELAY BEFORE TREATMENT

Theoretically, if all patients were subjected to resection as soon as carcinoma of the stomach developed, all would be cured. Early diagnosis is therefore of the utmost importance. A vivid illustration of this point is furnished by the following case:

F. C. (M.G.H. 61931), a 58-year-old man, entered the hospital on June 27, 1934, because he had vomited blood three times in the previous month. X-ray studies, including an upper gastrointestinal series, were negative. Gastroscopy showed chronic gastritis. Because of the possibility of carcinoma of the stomach, exploratory operation was performed. A 2-cm. lymph node, found on the greater curvature, on frozen section showed "highly malignant carcinoma." Because metastasis was already present, the surgeon did only a local excision of a small carcinoma of the greater curvature, and did not remove any other lymph nodes. The pathological report was adenocarcinoma. The patient was living and well 12 years later. Despite the high malignancy of the tumor and an inadequate operation, early surgery effected a cure.

Cancer of the stomach, once established, is usually a very rapidly growing tumor. This is shown by the rarity of cancers of the stomach discovered incidentally at post-mortem examination, when death is due to some other cause. This behavior is in contrast to that of carcinoma of the prostate, which is not uncommonly discovered in autopsy specimens as an incidental finding.

This behavior of carcinoma of the stomach has been recognized for many decades, and a vast amount of educational information has been spread by various cancer-control groups in an effort to bring the patient with gastric symptoms to the surgeon in time for cure. At the same time, the medical profession has become more alert to the problem, and early diagnosis has been facilitated by better x-ray films and an increased use of the gastroscope.

It seemed probable, therefore, that a comparison of the delay before treatment would show a significant decrease in this last decade. To obtain comparable series, the length of time that elapsed from the onset of gastric symptoms to the date that the patient entered the hospital for treatment was determined for all patients undergoing operation during the twenty-year period 1927 to 1946. The delay in the first ten-year period was then contrasted with that in the latter (Fig. 1). The remarkable and unhappy result is that the two curves can be almost exactly superimposed.

Why does the average delay before treatment still remain at the high level of five months? Is it apathy on the part of the patient or neglect by the physician? One is inclined to believe that all

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educational efforts have been negated by the radio and advertising columns with their promises of "relief for acid indigestion." Perhaps the medical profession should be satisfied that it is not fighting a losing battle against this propaganda, and conclude that if the public wishes to be cured of cancer of the stomach, it had better do something to aid itself.

No special attempt has been made in this study to discover the length of life of the untreated cases. It has been shown by Nathanson and Welch[3] and by Livingston and Pack[4] that the average duration

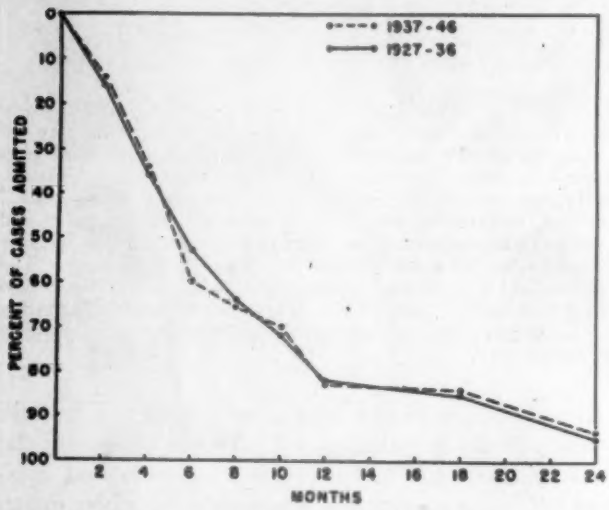

FIGURE 1. *Delay in Seeking Treatment among All Cases of Cancer of the Stomach in Which Operation Was Performed. The duration of symptoms before hospital admission is divided into ten-year periods.*

of life is about a year from onset of symptoms, and that 90 per cent of all patients are dead at the end of two years. The average delay from onset of symptoms to hospital entry of patients not subjected to surgery in the present series was about six months; at that time, operation was judged unwise or was refused by the patient.

Once the patient has been admitted to the hospital, he is studied completely. Endoscopy, as Benedict[5] has shown, is of great value, especially with lesions high in the stomach, since esophageal involvement may be observed. Peritoneoscopy is often valuable, especially if the patient has no symptoms of obstruction. If hepatic or peritoneal metastases are found, in the absence of obstruction, an operative procedure is contraindicated. On the other hand, if obstruction is present, the exploration is nearly always recommended, even if metastases are present, in the hope that a short-circuit may make the patient's life more comfortable.

The therapeutic procedures employed in the various periods are listed in Table 1.

THE PROBLEM OF GASTRIC ULCER

The well known fact that gastric cancer frequently simulates benign gastric ulcer needs re-emphasis. Allen and Welch,[6] in a review of gastric ulcers observed at the Massachusetts General Hospital from the years 1931–1940, found that 14 per cent of ulcers first considered to be benign were later proved to be malignant. No certain method could be found to differentiate the two types of lesions, but some conclusions were drawn that serve as a guide in therapy.

Immediate surgery is recommended in patients with a gastric ulceration under any one of the following conditions: if the ulcer is of short duration and the patient is over fifty years of age; if the ulcer is over 2.5 cm. in diameter; if there is no free hydrochloric acid in the stomach; if the ulcer is in the greater curvature or on the prepyloric region; and if the ulcer is chronic or recurrent and on the lesser curvature. Hospital observation and medical treatment for one month are advised if the lesion is acute and in a young patient, is under 1 cm. in diameter and is in the lesser curvature or on the anterior or posterior wall. If, in the last group, healing is not complete in a month, surgery is advisable; if healing is complete, repeat observation should be made one month after discharge from the hospital.

TABLE 1. *Types of Therapy Employed in All Cases of Carcinoma of the Stomach.*

PERIOD	TOTAL NO. OF CASES	NO OPERATION	LAPAROTOMY ONLY	PALLIATIVE OPERATION	RESECTION
		NO. OF CASES	NO. OF CASES	NO. OF CASES	NO. OF CASES
1927–1931	296	115	55	58	68
1932–1936	395	135	88	69	103
1937–1941	375	95	73	36	171
1942–1946	457	105	85	22	245

Another method of determining the diagnosis is by means of the cytologic smear, according to Papanicolaou's[7] technic. Fresh gastric washings are precipitated and stained. If malignant cells are found, the diagnosis is almost surely carcinoma. On the other hand, with known cancer of the stomach, the smear will be positive in only about two thirds of the cases. Thus, in the Vincent Memorial laboratory, the results to date have been as follows: in 50 cases of gastric ulcer or cancer in which gastric smears were employed, 24 patients proved to have carcinoma of the stomach, and the smears were positive in 15; of 26 patients without cancer, the smear was reported positive in 1, who proved to have a benign ulcer.[8]

If these recommendations are followed, there will be no significant delay in the recognition of gastric cancers. Furthermore, the very rare case of cancer that will "heal" under the best medical therapy (we have had at least 2 cases in this hospital) will soon be discovered, for the ulceration will recur after the patient leaves the hospital.

That the differential diagnosis of ulcer and cancer is still difficult is attested by the fact that 11 per cent of all the resections in the patients in the present study were made with the preoperative diagnosis of benign gastric ulcer. Fortunately, the delay before operation has been diminished in this group, because it has become appreciated that gastric resection for gastric ulcer produces excellent results, as shown by St. John et al.[9] and Judd and Priestley.[10]

One may ask how many lives might be saved if all the gastric carcinomas in this group were recognized and surgery performed at an early date. Since about 25 patients with apparent gastric ulcer appear in a year in this hospital, of whom about 14 per cent have carcinomas, 3 or 4 patients will be subjected to an earlier resection. Since the five-year curability rate is at least 40 per cent in this group, at least one additional cure a year should be expected in this hospital by early resection. But it is imperative for the surgeon to realize that, even when he has the stomach in his hands, he cannot make the differential diagnosis between ulcer and cancer, and that he must carry out the proper operation for gastric cancer.

Extension of the Operative Procedure

Gastric resection for carcinoma originally involved no attempt to excise any tissue but that of the stomach itself. However, the importance of removal of the regional lymph nodes along the lesser and greater curvatures was soon recognized, since the earliest metastases are usually found there. A second feature was emphasized by Castleman,[11] who showed the frequency of invasion of the proximal centimeter of duodenum by cancer of the stomach; he found that extension rarely proceeded beyond this level. A third site of early extension pointed out by Ogilvie[12] and Allen[13] is the great omentum. Metastases there are not uncommon, and may be overlooked except on microscopical section.

These three areas — the regional lymph nodes, the proximal centimeter of duodenum and the great omentum — should be removed with every resection for cancer of the stomach in which cure is the objective. Of course, if disease is to be left behind in other spots inaccessible to surgical removal, and only a palliative resection is planned, there is no need to remove the omentum in every case, although it is usually better to do so. After a long experience with this procedure, we are convinced that it carries no hazard and may contribute to a smoother convalescence.

As a corollary to the concept that gastric ulcer should be considered to be cancer until the pathologist proves it to be benign, it follows that the same operation should be carried out for gastric ulcer as for gastric cancer — that is, the removal of regional lymph nodes, great omentum and proximal duodenum. There is nothing more distressing to the surgeon than to read the pathologist's report "carcinoma of the stomach; no lymph nodes are included with the specimen." Yet this happens all too frequently, and many patients who should have the best chances of cure are doomed because of an inadequate operation.

Proximal extension of carcinoma of the stomach to the cardia often requires the procedure of total gastrectomy. This operation, although mentioned in the previous report, was a surgical rarity at that time. The technic as subsequently developed and described by Allen[13] has been followed in this hospital. Since the patients subjected to the procedure usually have extensive tumors, the mortality rate is bound to be high, and the number of cures small. The postoperative life span, however, is often surprisingly long.

The operation of total gastrectomy, in addition to an increased postoperative mortality, has other undesirable features. After operation, it is difficult for many patients to maintain adequate nutrition, and an anemia of significant grade is not uncommon. Studies of patients who have had recurrence after subtotal resections for cancer usually show that metastatic involvement of lymph nodes is present but that the remaining stomach is uninvolved. For these reasons, we do not subscribe to Longmire's[14] theory that all patients with carcinoma of the stomach should be treated by total gastrectomy.

The operative attack on carcinoma of the stomach, has, in the past, been limited by inaccessible proximal extension of the growth into the esophagus and mediastinum. Although it was frequently possible to draw down 3 to 5 cm. of the esophagus and do a total abdominal gastrectomy, in many cases it was impossible to get an adequate margin above the tumor. Recently, Churchill[15] and Sweet,[16] in pioneer work in this hospital, have developed the technic of transthoracic gastrectomy. With this approach through the diaphragm, extension of the cancer into the esophagus is easily amenable to resection.

There are several organs that can be sacrificed, resection en bloc with the carcinoma of the stomach being used. Thus, the transverse colon, the pancreas, the spleen and rarely a local extension into the liver can be resected with the tumor. It is our experience that none of these patients will survive five years, but recurrence of the disease will be delayed.

There are, unfortunately, many areas of metastasis that cannot be removed surgically. Metastatic lymph nodes in the head of the pancreas about the superior mesenteric artery or about the hepatic artery are nearly always nonresectable. Whereas a regional-lymph-node dissection of the left gastric artery may be done, a cure is not to be expected if the nodes about the celiac axis are involved. Metastatic lesions in the liver, if demonstrable, are indicative of widespread involvement of the organ. Removal of visible hepatic metastases will not con-

tribute to the postoperative comfort of the patient or increase the five-year survival rate. Peritoneal metastases are likewise indicative of widespread lymphatic involvement; local removal is useless.

The question might be asked regarding the relative importance of these extensions of the operative procedure so far as the control of cancer of the stomach is concerned. Five-year survivals are not to be expected if other viscera are involved as well as the stomach, so that massive resections of multiple viscera should be considered of value only as palliative procedures. On the other hand, there are rare five-year survivals after total gastrectomy. Obviously, the transthoracic approach has opened a new field that cannot yet be appraised accurately.

Table 2. *Mortality with Various Types of Gastric Resection.*

Type of Operation	No. of Cases		Operative Deaths		Operative Mortality	
	1937–1941	1942–1946	1937–1941	1942–1946	1937–1941	1942–1946
					%	%
Abdominal approach:						
Subtotal palliative resection...	35	32	13	2	37	6
Subtotal resection for cure ...	96	99	11	3	11	3
Total resection	35	34	17	11	49	32
Transthoracic approach:						
Subtotal resection	4	48	2	2	50	4
Total resection	1	32	1	9	100	28
Totals	171	245	44	27		
Averages					26	11

Reduction of Postoperative Mortality

The method of increasing the number of five-year cures of cancer of the stomach that has heretofore seemed to offer the most promise has been the reduction of excessive postoperative mortality. Thus, in the period 1932 to 1936, the mortality of gastric resection for cancer was 25 per cent. If these patients had not died, the five-year cures following resection would have increased by the same percentage.

It is gratifying to note that the mortality of resections has declined appreciably in recent years. The factors that have contributed are chiefly improved anesthesia, more careful blood, protein and vitamin replacement and chemotherapy. The anesthetic agent now employed is most commonly ether, by intratracheal administration, although our choice in patients who are not to have the diaphragm opened is continuous novocain administered in the spinal area by the method of Arrowood and Foldes.[17]

Local and parenteral use of penicillin just before, during and after operation has contributed a great deal to a smooth convalescence. Especially in transthoracic approaches, Sweet[16] has found that the use of penicillin has practically eliminated the complication of empyema. It appears to be no less effective in the peritoneal cavity. For full effect, it should be started before operation and continued parenterally several days afterward. Sodium sulfadiazine was employed intravenously for some time before penicillin was available, and is still utilized in some cases. The sulfonamides cannot be used locally with safety, and, as a rule, they may be employed for only a short time because of the danger of renal complications.

Blood replacement has also played an important role. It is essential to remember that a normal red-cell count and hematocrit may be misleading in any given patient, since the blood volume may be low, as Lyons[18] has pointed out. Blood is now given very liberally, therefore, despite normal laboratory figures. Likewise, intravenous amigen or amino acids and vitamins are administered in large doses when indicated preoperatively and as a routine measure postoperatively.

A technical contribution of great importance is that of Allen and Donaldson,[19] who introduced the routine use of double jejunostomy after gastric resections. The proximal tube is led back through the gastroenterostomy, and the distal one serves as a jejunostomy for feeding. Thus, the stomach is decompressed postoperatively without the use of a Levine tube. Stomal obstruction, which occurred in about 1 out of 20 patients in the series of Allen and Welch,[20] is no longer to be feared as a complication.

Although pulmonary emboli have not been eliminated as a cause of death, they have been reduced in number in recent years by prophylactic ligation of the superficial femoral veins, by the method of Allen, Linton and Donaldson.[21] We believe that this procedure is indicated in any patient who has a curable lesion, preferably at the time of resection, or within forty-eight hours thereafter.

These advances in therapy have resulted in a definite decrease in the number of postoperative deaths. Table 2 and Figure 2 show that the percentage of postoperative deaths has consistently diminished although the operability has increased.

To determine the effect of postoperative mortality on the curability rate, it is necessary to divide the resections into various groups (Table 2). Subtotal resections "for cure" represent cases in which the

surgeon has removed all gross cancer from the abdomen, and is the group that actually contains nearly all the cured patients. "Palliative" subtotal resections include cases in which cancer is left behind in inaccessible areas at the time of resection; no cures are to be expected. With total gastrectomies five-year cures are very rare, whereas transthoracic gastrectomies have not been done long enough to evaluate the curability rate. Hence, only subtotal resections for cure need be considered.

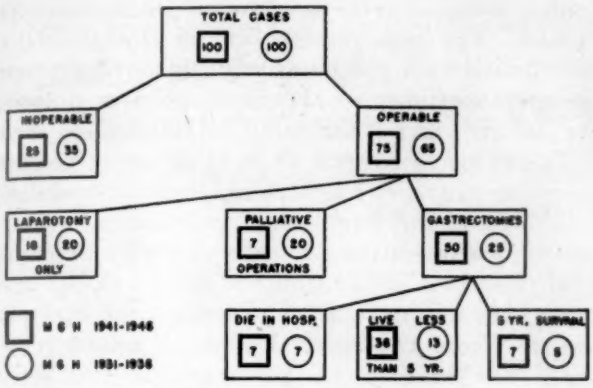

FIGURE 2. *Prognosis in Cancer of the Stomach.*
The fate of all patients entering the hospital with this diagnosis is demonstrated by decades.

The postoperative mortality in this group was 11 per cent in 1937 to 1941, and 3 per cent from 1942 to 1946. This means that the factor of postoperative mortality can, at present, no longer be reduced significantly, and that other methods must be found to increase the number of cures.

FIVE-YEAR SURVIVALS

What, then, is the ultimate fate of the patient who enters the hospital with carcinoma of the stomach? A graphic summary, comparing the results of the present decade with those of the last, is given in Figure 2, in which the results from 1927 to 1936 are shown by the circled figures. The results in the present series are included in the heavy squares. Incidentally, it may be noted that, in the last five-year series in which it was possible to determine end-result so far as five-year cures are concerned (1937 to 1941), only 4 patients have been untraced. They are considered in the tables to be dead of disease. Several trends are immediately discernible: the number of apparently operable patients has risen from 65 per cent to a level of 75 per cent; the patients who have an operation are much more likely to have a gastrectomy than they were before (50 per cent of all cases, compared with 25 per cent), whereas the percentages of exploratory laparotomies remain about the same and those of palliative operations other than gastrectomy have decreased; in the cases of gastrectomy, there is little change in the number of hospital deaths, and many more patients live up to four years after operation; and the over-all number of five-year cures has increased from about 5 per cent to 7 per cent.

It is clear that the great increase in the number of gastrectomies is due to the more widespread use of resection as the best palliative operation, even if all gross disease cannot be removed. The increased number of palliative resections has maintained the over-all mortality for resection at the same level as that of the previous study.

A further analysis of the gastrectomies performed is presented in Figure 3. There were no five-year survivals in the patients who had gross disease left in the abdomen, and only a rare five-year survival after total gastrectomy. Practically all the favorable cases fell into the group of subtotal resections, in which all gross cancer is removed.

The statement has sometimes been made that, even if gross cancer is left behind in the abdomen, a cure may result. Our information lends no credence to that claim. Eighty-five per cent of the patients with palliative subtotal gastrectomy were dead a year after operation, and all were dead two years after operation. The average postoperative length of life was about eight months.

Since the average length of life after exploratory laparotomy alone for cancer of the stomach is about six months, palliative gastric resections cannot be defended on the basis that a significant prolongation of life results. On the other hand, patients who have had an obstructing lesion removed are usually more comfortable and may die a relatively painless death from hepatic or pulmonary metastases. Since some patients without hope of cure are condemned to life for a period after operation, such a resection is really palliative. It seems justifiable to continue the use of the term "palliative gastrectomy" to distinguish operations in which gross disease is left behind in the abdomen.

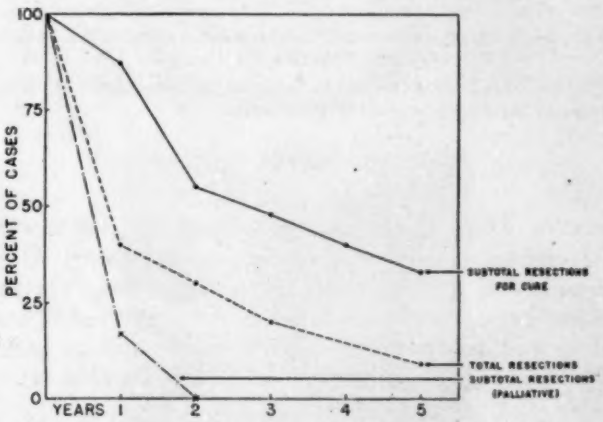

FIGURE 3. *Duration of Life after Various Types of Gastric Resections for Cancer (1937–1941).*

Livingston and Pack[4] have used the term "resectable cancer of the stomach" to describe cases in which all gross cancer can be excised. This is a valuable term, and in the present study is represented by all the subtotal resections, total resections and those done by the transthoracic route in which all gross disease can be removed. In the present series, the mortality for "resectable cancer" is 19 per cent, and the five-year curability is 20 per cent.

The prognosis of any case of carcinoma of the stomach may be gauged fairly accurately by microscopical examination of the specimen. The presence of metastasis to the regional lymph nodes is very

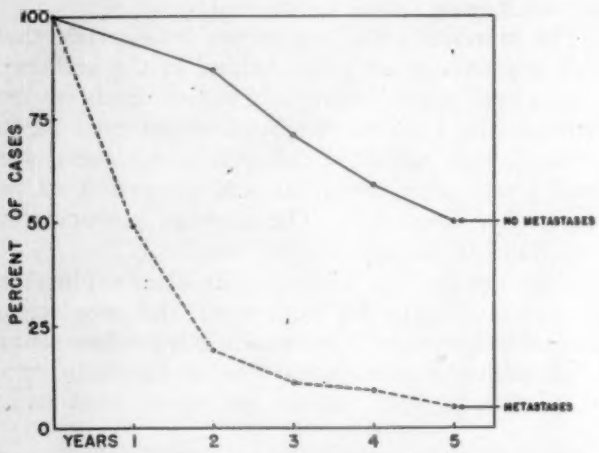

FIGURE 4. *Metastasis and Postoperative Duration of Life after Gastric Resection for Cancer.*

The end-results of all survivals indicate the importance of metastases in the determination of prognosis.

grave. Thus, in the years 1937 to 1941, there were 73 operative survivors who had metastases. Only 4 patients, or 5 per cent, lived five years. On the other hand, of the 42 patients who survived operation and had no extension to the regional nodes 20, or about 50 per cent, lived five years (Fig. 4).

Discussion

Livingston and Pack,[4] in their very complete survey of the treatment and end-results of gastric cancer, present many figures that are interesting to compare with this present series. It must be pointed out that their monograph was published in 1939 and that all clinics have improved their results since then. Thus, Pack[22] has recently reported that the operability in the Memorial Hospital has risen to 50 per cent. Therefore, no special credit need be taken by the Massachusetts General Hospital, except to point out that, here as well as elsewhere, modest gains have been registered in the therapy of cancer of the stomach.

Livingston and Pack state that there is no report in the literature in which the resectability was over 36.4 per cent and that the average rate was 18.7 per cent. Marshall and Welch,[23] in a recent report from the Lahey Clinic, found that 24.1 per cent of all patients with a diagnosis of cancer of the stomach in the years 1936 to 1940 had a resection. Somewhat similar figures were reported by Counseller[24] from the Mayo Clinic, where resection is carried out in 30 per cent of the patients with a diagnosis of gastric cancer. In our series, 50 per cent had resections; in 16 per cent inaccessible gross disease was left behind, whereas in 34 per cent all gross cancer was excised. The high resectability in this group has contributed to a comparatively high over-all postoperative mortality — 22 per cent. However, during the last five years of the study, although the resectability has increased from 45 to 54 per cent, the postoperative mortality has been reduced to 11 per cent.

Livingston and Pack also found that the average rate of postoperative five-year survivals from surgical treatment in the clinics studied was less than 2 per cent of the patients observed; the best rate reported from any surgical clinic or cancer center has never exceeded 5.2 per cent. In this series, from the years 1937 to 1941 (the last period available for end-results), there were 7 per cent five-year survivals.*

Summary

A study of all the patients with carcinoma of the stomach admitted to the Massachusetts General Hospital during the ten-year period 1937 to 1946 shows that the delay before treatment has remained unchanged, averaging five months. A more aggressive attitude toward gastric ulcer has increased the recognition of early cancer of the stomach.

The introduction of a transthoracic approach and the wider use of total abdominal gastrectomy have increased the number of cases available for resection.

The mortality for gastric resections for cancer has dropped to a present level of 17 per cent for the entire series and to 11 per cent in the last five-year period. The mortality of subtotal resections in which all gross disease is removed has been 3 per cent in the last five-year period.

Meanwhile, the number of unoperated patients has declined so that 75 per cent have an operation. Fifty per cent of the total have a gastrectomy, either subtotal or total.

The best palliative operation, if gross disease cannot be removed, is subtotal gastrectomy.

The five-year survival rate is now 7 per cent of the entire group that enters the hospital.

The most fruitful method now available to increase the number of cures of cancer of the stomach

*Since this article was submitted for publication, State, Moore and Wangensteen[25] have surveyed the patients with carcinoma of the stomach entering the University of Minnesota Hospital from 1936 to 1945. Their figures show a 55.2 per cent resectability, with a mortality of 16.6 per cent, and an over-all five-year salvage of 6.6 per cent.

is to reduce the delay from onset of symptoms to surgical intervention.

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COMPLETE HEART BLOCK*

A Study of Two Cases in Veterans of World War II

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A NUMBER of reports in the medical literature emphasize the fact that some patients with complete heart block may have a favorable prognosis regarding life and the ability to perform daily tasks. In nearly every case the conduction defect is thought to be congenital in origin. Campbell,[1] in his discussion of congenital complete heart block, states that, "if there are no complications carrying special risks of their own, the prognosis is good and will probably prove that the condition is compatible with survival to old age." The cases reported below emphasize the ability of people affected with this malady to lead normal lives and at times to undergo rather strenuous exertion without demonstrable ill effects. Both patients were veterans of World War II. Only 1 case is reported in the literature in which a patient with complete heart block, apparently congenital in origin, was a member of the armed forces.[1]

Case Reports

CASE 1. A 34-year-old man reported to the Out-Patient Department on June 11, 1947, for compensation examination because of complete heart block. He had been inducted into the service on December 7, 1943. Preinduction physical examination had revealed a resting pulse rate of 54, rising to 80 on exercise. The remaining examination revealed no abnormalities. After induction he completed 8 weeks of basic training. During a routine screening examination, a systolic apical murmur was heard, and the patient

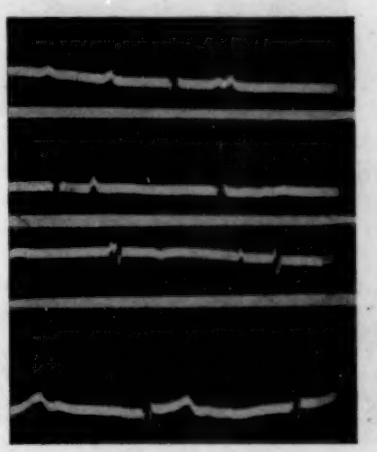

FIGURE 1. *Tracing Obtained in Case 1 on May 15, 1943, Showing Complete Auriculoventricular Dissociation, with an Auricular Rate between 53 and 60 and a Ventricular Rate of 43. The T waves are upright in Lead 1, diphasic in Lead 2 and inverted in Lead 3. The T waves in Lead F_4 are upright.*

was hospitalized for observation. An electrocardiogram taken on May 15 had shown complete heart block, with a diphasic T wave in Lead 1, inverted T waves in Leads 2 and 3 and an upright T wave in Lead 4 (Fig. 1). No other

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significant abnormality had been demonstrated during the study. The patient had been discharged from the service on June 5 and had subsequently been employed as a night clerk in a hotel, where he performed general manual labor.

The past history revealed a normal birth after a normal period of gestation. As a child the patient had measles, mumps, chicken pox and pertussis. At the age of 23, while playing baseball, he suddenly fainted. Since that time he had experienced six similar episodes, the last occurring at the age of 28 years. Additional medical history revealed that when the patient was 25 years old he had been told that he had a "bad heart." There was no history of scarlet fever, rheumatic fever, tuberculosis, syphilis or diabetes. The patient had attended school until he was 13 years old. At that time he completed the sixth grade; he incurred no difficulty in learning, but his schooling was stopped owing to the death of his father, whose position as a bread winner the patient accepted. At first he worked as a farm hand and later as a laborer on a railroad. He also held a job in a canning factory and finally was employed as a guard in a defense plant. He had no difficulty performing any of these tasks.

The family history was irrelevant.

Physical examination revealed a well developed and well nourished man who appeared to be in excellent health. The height was 69 inches, and the weight 175 pounds. An exercise tolerance test, consisting of stepping on and off a chair 18 inches high twenty-five times, caused only a mild dyspnea. Examination of the heart showed no enlargement. There was a Grade I, blowing, systolic apical murmur transmitted only slightly toward the sternum. The murmur was somewhat accentuated by exercise. The remainder of the physical examination disclosed nothing of note.

The blood pressure was 120/80. The resting pulse was 52, rising to 80 after exercise.

Examination of the blood disclosed a red-cell count of 4,450,000 and a white-cell count of 6000, with 66 per cent neutrophils and 34 per cent lymphocytes. The sedimentation rate was 1 mm. in 1 hour.

Fluoroscopic examination of the heart showed the cardiac silhouette to be normal in size and shape.

An electrocardiogram revealed a complete heart block, with a diphasic T wave in Lead 1 and inverted T waves in Leads 2, 3 and F_4 (Fig. 2).

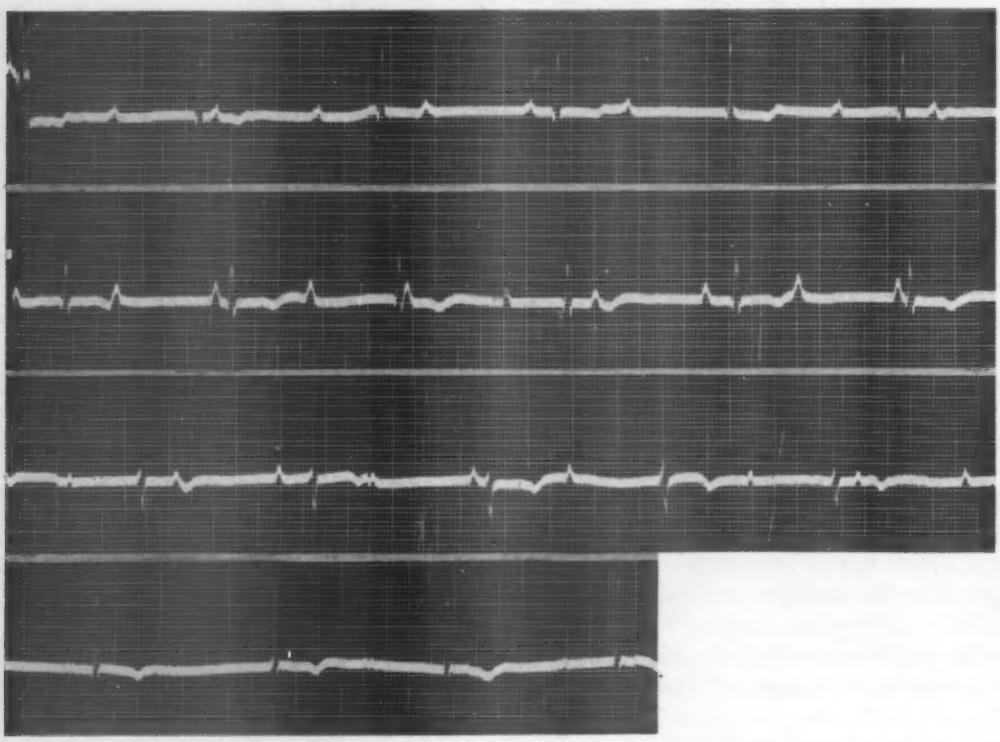

FIGURE 2. *Electrocardiogram Obtained in Case 1 on June 11, 1947, Showing Complete Heart Block. Note the T-wave changes that have taken place since the last observation.*

CASE 2. A 19-year-old veteran reported to the Out-Patient Department for treatment because of "heart trouble" and "weakness."

The patient had been a premature baby and had supposedly weighed only 5 pounds at birth. A further developmental history did not reveal anything unusual. The patient had had measles, mumps, whooping cough and chicken pox. After the period of childhood, except for occasional sore throat, he had never been sick. There was no history of scarlet fever, rheumatic fever, tuberculosis, diphtheria or syphilis. He gave a history of two syncopal attacks, both occurring at the pre-school age. No details concerning these episodes were obtainable. While in school he had no difficulty keeping up with other children. He was a member of the high-school basketball team. After completing 2 years of high-school education, he went to work for a packing company. This called for arduous manual labor, which he was able to perform without any ill effects. His next job was that of a truck driver. He subsequently passed a physical examination for a Civil Service position, which he held until his enlistment in the United States Navy on January 5, 1945. Physical examination performed prior to enlistment showed a pulse rate of 48, which increased to 56 with exercise. The remainder of the examination was reported as showing nothing of note. The patient was accepted for duty with the Navy and had no difficulty until April 25, 1945, when he reported to sick bay because of an upper respiratory infection. At the time of admission to the hospital the pulse rate was 44, "increasing only slightly with exercise." A diagnosis of complete heart block was made, the diagnosis being confirmed by a number of electrocardiographic tracings. The patient was discharged from the service on July 10 and subsequently re-

turned to his old job, that of a truck driver. He was unable to perform his duties as well as he did before he entered the Navy because, as he put it, "he felt weak all over."

The family history was of no consequence.

Physical examination disclosed a patient of hypasthenic habitus. He did not appear either acutely or chronically ill. An exercise-tolerance test consisting of stepping on and off a chair 18 inches high revealed only a mild dyspnea. Examination of the heart disclosed some enlargement to the left, the left border of cardiac dullness being slightly outside the midclavicular line. No thrills were palpable either before or after exercise. There was a Grade II, blowing systolic murmur, which was best heard in the third and fourth interspaces just to the left of the sternum. This murmur was transmitted toward the apex and was somewhat accentuated by exercise. The remainder of the examination was negative.

The pulse rate was 40, regularly increasing to 52 with exercise. The blood pressure was 140/70.

Fluoroscopic examination showed a mild enlargement of both the right and left ventricles.

An electrocardiogram revealed a complete heart block (Fig. 3).

FIGURE 3. *Electrocardiogram in Case 2, Showing Complete Heart Block, with an Auricular Rate of Approximately 60 and a Ventricular Rate of 33.3. No other significant abnormalities are noted.*

DISCUSSION

It is true that the etiology of the heart block in the cases reported above is open to question. However, the following findings strongly suggested the congenital origin of the conduction defect: the absence of an acquired etiologic agent that is known to affect the myocardium; the ability of the patients to lead normal lives and at times to undergo rather strenuous exertion without demonstrable ill effects; and the presence of a relatively faster pulse rate as compared with acquired complete heart block. The study of the 2 subjects revealed some evidence that may justifiably be construed as indicative of disease of the heart other than the conduction defect. In Case 1 there was an associated progressive inversion of the T waves in Leads 1, 2, 3 and F_4. This may have been due to some obscure pathologic process, possibly infectious in origin, involving the myocardium or the pericardium, or both, or to a process involving the coronary arteries. No definite conclusion can be reached at present. In Case 2 the systolic murmur coupled with the enlargement of the heart might perhaps be ascribed to the increased stroke volume associated with the slow heart rate.

A review of the literature regarding congenital complete heart block showed a lack of uniform criteria to which a case must conform before it may be assumed to be congenital in origin. Yater,[2] in a review of this subject in 1929, pointed out certain requirements that should be fulfilled before a diagnosis of congenital complete heart block can be made. These are as follows: electrocardiographic proof of heart block; a record of a slow pulse at an early age; and absence of a history of infection, especially diphtheria, rheumatic fever, chorea or congenital syphilis. He also stated that syncopal

attacks at a fairly early age and the presence of other congenital heart lesions add weight to the congenital etiology of the heart block. Most writers assume that complete heart block in children and young adults is to be considered infectious in origin until proved otherwise. Recently, different ideas were expressed.[1, 3] Leys[4] points out that permanent complete heart block following infection is rare and also states that the burden of proof lies on the shoulders of the one who assumes that a case of complete heart block in young adults is due to infection. White[5] asserts that permanent heart block following an acute infectious process is rare and that the most frequent cause of complete heart block is coronary-artery disease. Campbell,[6] in a review of 64 cases of complete heart block, found that 13 per cent were congenital in origin, and slightly over 10 per cent could be accounted for by syphilis and rheumatic fever. Seventy-five per cent of the cases were due to coronary-artery disease.

Subjective complaints caused by congenital complete heart block are few. A small percentage of the patients experience Stokes–Adams attacks or shortness of breath, or both, on moderate exertion. Others develop neurasthenia after learning about their malady.

Yater[2] calls attention to the relative infrequency of cyanosis in these patients. When cyanosis is found, it is probably due to an accompanying heart lesion rather than to the heart block per se. Physical examination usually reveals a pulse rate of 40 to 50 and an enlarged heart. This cardiac enlargement may be attributed to an associated heart lesion or to prolonged diastolic filling due to slow heart rate.

It is of great practical importance to differentiate congenital complete heart block from the acquired condition, for the prognosis for life and the capacity to lead normal lives is good in congenital heart block. In a series of 8 cases that Campbell[1] followed for nine years he reported 2 deaths. The average survival rate for the other 6 patients was twenty-two years on last examination. The ages of these patients ranged from twenty-two to forty-two years. Jaleski and Morrison[7] reported a case in a thirty-one-year-old woman with congenital complete heart block who went through two terms of pregnancy and delivery without any complications. Levine[8] mentions a fifty-five-year-old patient who was known to have had complete heart block since the age of six, probably of congenital origin. The optimistic outlook in congenital complete heart block mentioned above should be contrasted with life expectancy in acquired heart block. The studies of Campbell[6] and Graybiel and White[9] show that approximately 70 per cent of patients with acquired heart block died less than three years after the discovery of the lesion. The remaining 30 per cent were alive after an average of six to seven years.

Summary

Two cases of complete heart block, probably congenital in origin, in veterans of World War II are presented.

The significant clinical aspects of congenital complete heart block are discussed.

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VACCINATION AGAINST INFLUENZA A AND B*

A Comparison of Reactions, Doses and Titer Responses of Two Different Vaccines in Infants and Children

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ALTHOUGH numerous investigators have reported success in protecting adults from influenza A and B, very few studies are available in infants and children. A quantitative evaluation of the titer responses in this age group to various doses and types of vaccines was undertaken, as well as a study of the local and systemic reactions to the vaccines. Adams, Thigpen and Rickard[1] showed that the immune response to influenza A infection was equally great in young infants and older children.

A group of 245 children, ranging in age from one to sixteen years and interned in one building for residua of poliomyelitis, were the subjects of this study. The children were divided into five groups, all of which were nearly comparable in age distribution. The first two groups received 0.5-cc. and 1-cc. doses of vaccine 1.¶ The second two groups received the same doses of vaccine 2.‖ The fifth group was not vaccinated, but early and later serum titer studies were done as in the first four groups. This study was carried out in November and December, 1946.

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¶This vaccine, which was prepared from egg cultures of influenza A (PR 8 and Weiss strains) and B (Lee strain) viruses by erythrocyte adsorption and elution, was kindly supplied by Eli Lilly and Company, Indianapolis, Indiana.

‖This vaccine, which was prepared from egg cultures of influenza A (PR 8 and Weiss strains) and B (Lee strain) viruses by calcium phosphate adsorption, was kindly supplied by Parke, Davis and Company, Detroit, Michigan.

Method

The inoculations of vaccine were given subcutaneously from 9 to 10 a.m. Temperatures were taken at four-hour intervals, and changes were computed by comparison with the patient's previous temperature record. The maximum rise was determined in each of 186 cases, as well as the mean maximum for each group.

The local reaction was evaluated immediately, and at intervals of approximately twenty-four hours for thirty days.

Samples of blood were obtained before the vaccine was given and fourteen days after its administration. The viruses used in the quantitative titer determinations were those of influenza A (PR 8 strain) and influenza B (Lee strain). The photoelectric densitometer was employed after the method described by Hirst and Pickels.[2] All the four hundred and fifty-six determinations were done in pairs and in large lots.

Table 1. *Temperature Elevations.*

Vaccine	Dose	Mean of Maximum Elevations	Range of Maximum Elevations	Subjects with Slight Elevations*		Subjects with Moderate Elevations†		Subjects with Marked Elevations‡	
	cc.	°F.	°F.	no.	per-centage	no.	per-centage	no.	per-centage
1	0.5	1.19	−0.2 to +4.6	25	53	17	36	5	11
2	0.5	0.48	−0.4 to +1.6	34	79	9	21	0	0
1	1.0	1.12	−0.2 to +4.0	30	60	15	30	5	10
2	1.0	0.59	−0.4 to +4.0	35	76	10	22	1	2

*Less than 1°F.
†1.0 to 2.9°F.
‡3°F. or higher.

Results

Temperature

The means of the maximum temperature elevations are presented in Table 1. The values show that 0.5 cc. of a vaccine gave the same average temperature rise as 1 cc. of the same vaccine. Vaccine 1 caused a significantly higher temperature response than vaccine 2. Many children receiving the former had temperatures well over 100°F. The maximum temperature elevation occurred most frequently eight to twelve hours after vaccination.

Local Reaction

The injection of vaccine 1 caused a sharp, stinging pain, which lasted a few minutes and then subsided.

Vaccine 2 caused little or no immediate pain. The local reaction was measured and palpated at intervals, and although there was considerable variation, the following general observations were made: twenty-four hours after the injection of vaccine 1 there was a small area (1 or 2 cm.) of erythema, which was slightly swollen and indurated and moderately tender. At forty-eight hours there was usually minimal or no local reaction remaining. Twenty-four hours after the administration of vaccine 2 there was an area of erythema, which, on the average, was significantly larger (2 to 10 cm.) than that caused by vaccine 1. Also, the local site was usually more swollen and indurated, and in a few subjects the whole upper arm was tender. At the end of forty-eight hours a definite subcutaneous nodule had formed in most of the subjects receiving vaccine 2. This was still present thirty days later in a few cases.

TABLE 2. *Frequency of Systemic Reactions to Influenza Vaccine.*

VACCINE	DOSE	TOTAL NO. OF SUBJECTS	SUBJECTS WITH REACTIONS	
	cc.		NO.	PERCENTAGE
1	0.5	39	11	28
2	0.5	48	3	6
1	1.0	49	10	20
2	1.0	48	8	17

Systemic Reactions

The number of systemic reactions is recorded in Table 2. The ages of the children with reactions ranged from thirteen months to nine years in the group given 0.5 cc. of vaccine 1, three to thirteen years in the group given 0.5 cc. of vaccine 2, sixteen months to sixteen years in the group given 1 cc. of vaccine 1 and two to fifteen years in the group given 1 cc. of vaccine 2. The principal reactions were headache, restlessness and wakefulness. In general it was concluded that severer, as well as more frequent, reactions were observed with vaccine 1. The least number of systemic reactions occurred with 0.5 cc. of vaccine 2. A convulsion occurred in a one-year-old girl who received 1 cc. of vaccine 1.

No unquestionably positive reaction was observed in any of the 60 children who were given skin tests. Difficulty in interpreting skin tests with the undiluted vaccine was encountered because of the irritative properties of the formalin contained in the material used. (None of these subjects are included in the titer studies.) Curphey[3] has reported a fatal allergic reaction to influenza vaccine. Ratner and Untracht[4] cited several allergic reactions and recommend that all patients be tested with 0.02 cc. of the undiluted vaccine before vaccination. Protamine-precipitated vaccine,[5] like that of calcium phosphate adsorbed, apparently contains less allergenic substance than the vaccine prepared by erythrocyte adsorption. A newer vaccine prepared by centrifugation[6] is said to be virtually free of substances causing allergic reactions.

Antibody Titers

The increase in the antibody titer is indicated by the ratio of the late to the early value rather than by an absolute arithmetic increase. Table 3 shows the frequency distribution of all the cases in terms of the number of fold increase of the late titer over the early titer (late to early ratio).

TABLE 3. *Frequency Distribution of Titer Ratios.*

VACCINE	DOSE	INFLUENZA VIRUS	SUBJECTS WITH INCREASE OF LATE OVER EARLY TITER				TOTAL NO. OF TITER PAIRS	GEOMETRIC MEANS OF INCREASES
	cc.		LESS THAN 2 FOLD	2 TO 3.9 FOLD	4 TO 7.9 FOLD	8 TO 50 FOLD		
1	0.5	A	14	3*	7	3	27*	2.4 fold
2	0.5	A	14	5	1	2	22	3.5 fold
1	0.5	B	8	8	6	5	27	1.9 fold
2	0.5	B	9	7	2	4	22	2.9 fold
1	1.0	A	11	7	3	1	22	2.1 fold
2	1.0	A	5	3	4	2	14	4.1 fold
1	1.0	B	4	6	6	5	21	3.0 fold
2	1.0	B	1	2	3	7	13	7.8 fold
(Control)		A	30	0	0	0	30	1.0 fold
(Control)		B	30	0	0	0	30	1.0 fold†

*Of the 27 titer pairs against influenza A in the group receiving 0.5 cc. of vaccine 1, there were 3 with late titers showing an increased range of 2 to 3.9 fold over the early titers.

†1.0 fold represents no increase in the late over the early titer.

In view of the fact that the titers increase in a geometric fashion, the geometric mean was employed in the group comparisons, and the statistical calculations were made on the basis of logarithms. The geometric means for the titer increases are included in Table 3. All the means in the groups receiving vaccine were significantly higher than those in the control group. Except for the mean increase of 7.84 against the virus of influenza B in the group receiving 1 cc. of vaccine 2, in which the number of patients was too small and the range of values too great to justify an accurate comparison, there was no significant difference

between the groups. For example, 1 cc. of a vaccine was no better than 0.5 cc. of the same vaccine, nor was vaccine 1 better than vaccine 2 from this point of view. There did not appear to be any differences in the titer response of the younger compared to the older children. The titers against the virus of influenza B were generally higher than those against the virus of influenza A.

Discussion

The subjects in our study were not exposed to an epidemic of influenza, so that the value of the vaccinations was not tested clinically. A fairly consistent rise in antibody titers was demonstrated in the majority of the vaccinated group as opposed to the controls. Henle, Henle and Stokes[7] have shown greater protection against the disease in the persons with the high titers. The majority of the subjects whose titers failed to rise appreciably (less than twofold) had high initial levels.

All the inoculations were given subcutaneously. Van Gelder and his associates[8] concluded that the intracutaneous route produced better titer responses. No subject in our study received more than one injection. The antibody level reached after one dose was as high as that observed after two doses according to a study reported by Hare and his co-workers.[9]

The second blood sample was drawn after fourteen days in all subjects. These titers probably did not represent the maximum level in each case because of varying host responses as well as the differences in vaccines used.

In our experience, the vaccines employed were safe for infants and children in the doses employed, and with one exception, in which a large dose was given to a one-year-old child, no severe reactions were observed in the 245 subjects. The question of the use of influenza vaccine in the practice of medicine remains for the individual physician to answer. Certainly, it may be offered as giving protection of some degree to most persons, since its value has now been attested by several reports, including that of the Army Influenza Commission.[10] The administration of any vaccine entails an occasional unfavorable reaction. Whether or not this militates against its use in practice cannot be decided here, but its value as a public-health measure can hardly be questioned when the morbidity and mortality figures in large cities after influenza epidemics are studied. The uncomplicated disease except for pandemics probably is not responsible for death, but it is one of the common precursors of pneumonia, which takes its toll after every influenza epidemic. The pandemics of influenza recorded in medical history have been responsible for more deaths than any scourge known to man. One of the probable causes of pandemics is a world-wide susceptibility. It seems possible that extensive use of influenza A and B vaccine will offer man some protection against pandemic as well as epidemic influenza and against the high mortality associated with this disease.

Summary

A comparative study of reactions, doses and antibody titers has been made with two different vaccines against influenza A and B in infants and children.

The temperature elevations were significantly higher with vaccine 1 than with vaccine 2, although the dose of the vaccines did not appear to make any appreciable difference. Vaccine 2 caused more local reactions, such as swelling and tenderness at the site of inoculation, whereas the systemic reactions appeared to be more intense with vaccine 1.

A definite increase in the antibody titers was demonstrated in the majority of the vaccinated subjects as compared to the controls, but no significant difference between the vaccines was observed.

There was no significant difference between the titers obtained with 0.5 cc. and 1 cc. of the same vaccine. Children under three years of age, in our opinion, should not be given more than 0.5 cc. of vaccine.

The decision whether or not to use influenza vaccine is left to the individual physician.

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ACUTE MENINGITIS CAUSED BY *NEISSERIA SICCA**

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THE gram-negative diplococci such as *Neisseria catarrhalis* and *N. sicca*, commonly found in the pharynx, rarely cause meningitis. However, upon occasions they have been proved to be the sole cause of the disease.[1–10] The following case of meningitis due to *N. sicca* was proved by culture and serologic examination.§

R. L., a 6½-year-old boy, entered the hospital on January 20, 1947, with a history of sore throat, frontal headache, fever and vomiting of 24 hours' duration. The temperature had risen to 104°F., the headache had increased in severity and he had developed a stiff neck a few hours before admission. The patient had received several doses of sulfadiazine at home, but most of this had been lost in the vomitus.

The past and family histories were noncontributory except for left internal strabismus since infancy.

Physical examination revealed a well developed and well nourished child, who was drowsy but conscious and cooperative. There were no abnormal eye findings except for the left internal strabismus. The fundi were normal. Definite spinal and nuchal rigidity were elicited. The mucous membrane of the throat was somewhat inflamed. The ears were normal. The posterior cervical lymph nodes were slightly enlarged. No petechiae were noted. A bilateral Kernig reflex was present. The blood pressure was 100/70.

Examination of the blood showed a red-cell count of 3,930,000 and a white-cell count of 15,200, with 86 per cent neutrophils, 12 per cent lymphocytes and 2 per cent eosinophils. A blood culture was negative, as was a tuberculin patch test. An x-ray film of the chest was normal. The blood sulfadiazine level ranged from 9 to 15 mg. per 100 cc. A lumbar puncture was done and 10 cc. of cloudy spinal fluid, under increased pressure, was obtained. The initial pressure was equivalent to 280 mm. of water; the dynamics were normal. Examination of the spinal fluid disclosed a white-cell count of 4150, with 84 per cent polymorphonuclear leukocytes, 16 per cent lymphocytes and a total protein of 80 mg., sugar of 83 mg. and chloride of 720 mg. per 100 cc. A direct smear demonstrated many pus cells but no organisms; a culture showed *N. sicca*.

As soon as the diagnosis of meningitis had been established the patient was given sodium sulfadiazine intravenously and penicillin intramuscularly. Because the previous vomiting had resulted in some dehydration, 5 per cent glucose in physiologic saline solution with 1/6 molar lactate was given intravenously. In the evening of the 2nd hospital day, the urine was noted to be grossly bloody, and sodium sulfadiazine was therefore discontinued. Streptomycin (125,000 units every 3 hours) was started, and 1/6 molar lactate was continued intravenously to keep the urine alkaline — 24 hours later the urine was free of blood.

On the day after admission the patient showed considerable improvement, and he was able to retain food. Penicillin was given intrathecally (5000 units in 5 cc. of physiologic saline solution) on the 2nd and 3rd days. The urine contained red cells on the 3rd hospital day but was normal thereafter. On the 4th hospital day, there were no clinical signs of meningitis. Streptomycin was discontinued, and at that time oral glucosulfadiazine was given without any further untoward effect. The patient continued to improve. Penicillin was discontinued on the 9th, and glucosulfadiazine on the 11th hospital day. The spinal fluid on discharge was clear, with 4 white cells per cubic millimeter, 100 per cent lymphocytes, a sugar of 49 mg. per 100 cc. and a total protein of 36 mg. per 100 cc.; culture was negative.

Serum agglutination with *N. sicca* demonstrated a positive titer in a dilution of 1:384 (control, negative) 12 days and one of 1:384 (control 1:96) 61 days after the onset of the acute illness. The titer was negative for both patient and control 154 days after the onset.

DISCUSSION

The initial diagnosis in this case was meningococcal meningitis, in view of the presence of clinical meningitis with cloudy spinal fluid, which on direct smear showed many pus cells but no organisms. The diagnosis was further strengthened by the report of the presence of a gram-negative diplococcus obtained from the culture of the spinal fluid. However, the laboratory soon reported that the organism isolated did not agglutinate with any of the strains of meningococci available. Subsequently, this organism was identified by the laboratory of the Worcester Public Health Department and confirmed by the laboratory of the Massachusetts Department of Public Health as *N. sicca*.

The possibility of contamination of the spinal fluid was entertained, but on inquiry it was found that this organism is a very rare contaminant.[11]

The question of determining whether the patient had developed immune bodies to this organism was then investigated. Because *N. sicca* tends to clump spontaneously in the presence of physiologic saline solution, the antigen was prepared by a special method to minimize this phenomenon. The organism was grown on nutrient agar slants and incubated at 35°C. for forty-eight hours. The slants were washed off with tap water as a precautionary measure to avoid automatic precipitation of the organism. The harvest was collected and ground up with fine sand,¶ and the suspension was allowed to stand for one hour. The supernatant fluid was decanted through cotton, and the suspension diluted with tap water to a No. 8 McFarland nephelometer standard of approximately 2,400,000,000 organisms per cubic centimeter. The antigen was then killed at 60°C. for one hour. No preservative was added. The routine slow macroscopic tube agglutination test was used, as described by Kolmer and Boerner.[12] Inasmuch as there was a small but definitely noticeable amount of antigen precipitation in tap water, a positive reaction was assigned only to tubes that showed marked clearing with the formation of large flakes.

It will be noted that twelve and sixty-one days after the onset of acute symptoms, the organism

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was agglutinated by the patient's serum in a dilution of 1:384. Approximately five months after the illness the titer had dropped to a normal level. The control serums were presumed to be normal and were obtained from men between the ages of twenty and twenty-three years. The finding of a titer of 1:96 in one of the control serums cannot be definitely explained, except by the fact that the control subject may have had a recent infection with *N. sicca*.

On review of the literature it was found that meningitis due to *N. sicca* has been reported only in the course of an endocarditis caused by this organism.[5–7, 10, 13] In the 5 reported cases of endocarditis, symptoms of meningitis occurred in 3, and a positive spinal-fluid culture was found in 1.[7] All these cases of endocarditis terminated fatally except 1 in which recovery followed the use of heparin and sulfapyridine.[6]

Several cases of meningitis caused by *N. catarrhalis* have been reported[1, 9] and also some cases caused by atypical Neisseria.[2, 3, 4, 8, 10] The comparative rarity of meningitis caused by this group of organisms suggests a low pathogenicity but modifies the older concept of this group as nonpathogenic.[14]

Summary

A case of acute meningitis caused by *Neisseria sicca* is reported. The organism isolated was identified by two different laboratories. An attempt was made to determine the titer of antibodies in the patient's serum, cultures of the organism being used as the antigen. Although the serologic method available was not entirely satisfactory because of the characteristics of this organism to clump spontaneously, significant titers indicating antibody formation were obtained. Approximately five months after the onset of the acute disease, the titer had dropped to a normal level.

It is believed that this is the first straightforward case of acute meningitis caused by *N. sicca* and uncomplicated by any other infectious process such as endocarditis described in the literature.

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MEDICAL PROGRESS

CANCER

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As a result of public interest, large sums of money have become available in the field of cancer, from state and federal sources and from charitable foundations, and it seems probable that the interest and funds will continue for a long time. The money has been used for stimulation of research, for cancer education among the laity and the medical profession and for direct service to the patient in the form of improved diagnostic and therapeutic facilities.

RESEARCH

The literature of laboratory cancer research has become so voluminous that it is virtually impossible for anyone to undertake to digest it all. The Fourth International Cancer Research Congress presented representative contributions in all the principal fields of investigation. Cowdry's[1] recent summary of the Congress ably recapitulates the major fields of interest.

EDUCATION

Undergraduate

Although a considerable part of a medical-school curriculum deals with cancer, and with basic sciences essential to an understanding of cancer, it is true that in many medical schools there has been little or no attempt to correlate the various components in such a way as to give the student a coherent conception of cancer. A committee of the National Advisory Cancer Council has urged the desirability of co-ordinating the teaching of cancer in medical schools, offering financial support for schools presenting acceptable plans of instruction. Several schools have already adopted the recommendations of the committee, and it is anticipated that others will recognize the merits of the proposals.

Graduate

Fellowships offered by the National Advisory Cancer Council are intended to train men at the resident level to be cancer specialists. The rather rigid requirements of training in surgery, radiology and pathology make it difficult for many hospitals to fit these fellowships into existing resident training programs. In addition, the fellowships come into conflict with the requirements of many of the specialty certification boards. Some relaxation and elasticity of the program would probably result in better training of more men.

The American College of Surgeons, at the annual clinical congress and in the sectional meetings, offers special sessions and symposia in cancer. These meetings bring to a large audience a condensed review of recent important advances in the cancer field. The series of special articles appearing in the *Journal of the American Medical Association*,[2] with the co-operation of the American Cancer Society, is designed to bring a concise presentation of cancer subjects to the general practitioner. These articles will be assembled in a book, which will assure their preservation.[3] The announcement of a new journal *Cancer*, under the sponsorship of the American Cancer Society, to include a thorough abstract section in addition to original contributions, is welcome news to all who are working in this field.

Public

Lay education in cancer has been promoted by various groups, notably by the Women's Field Army of the American Cancer Society. There can be no question that as a result of such education, many patients seek medical advice earlier than they would have done otherwise. They are also likely to require a more thorough examination from their physician. Indeed, the demands of the laity have emphasized the necessity for improved cancer teaching for the profession. The public interest stimulated by lay education has in large measure helped to make available the funds referred to above, and to some degree has given the laity a voice in the projects for which the money is used. The public demand has also been responsible for the development of detection clinics.

DETECTION CENTERS

It is a basic postulate that the earlier a cancer is detected and treated, the greater is the likelihood of cure. It is also true that the earliest stages of most cancers give rise to no symptoms. Thus, it would be desirable to have some test to which the apparently healthy person could be submitted that would detect cancer in its earliest stages. The only present test that can be employed is a complete and thorough examination. The more thorough the examination, the greater is the likelihood that cancer will be detected in its early stages. Practical considerations of time, personnel and expense impose

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limitations on the thoroughness of the examination. It is apparent that the initial examination must be relatively brief and inexpensive, and that this preliminary screening may be expected to segregate for more extensive study the group most likely to show positive findings.

In regular medical practice the most significant finding on screening is the presence of a symptom or symptoms. Indeed, a patient in general exercises this screening test and consults a physician or goes to a clinic because of a symptom. The physician can then carry out the more thorough investigation necessary to discover the cause of the symptoms. In doing so, he may uncover cancer or some other disease. Without the stimulus of symptoms to be explained, examinations may become perfunctory or routine. Statistics must be available regarding the number of cases of cancer found during the routine physical examinations of applicants for life insurance or of men selected for military service. Statistics are available concerning the expected incidence of cancer in various age groups at a given time.[4]

In response to public pressure, under the sponsorship of various foundations, numerous centers have been established for the detection of cancer. The American College of Surgeons has defined standards for these centers and gives approval to those complying with the standards.[5] Most of the centers report a much higher incidence of cancer than the calculated expected frequency.[6] It is probable that this is due to the inclusion of a large number of persons who are not in fact free from symptoms, and that the centers are serving to this extent as cancer clinics rather than as detection centers.

The centers also reveal a very great number of other conditions requiring medical treatment.[7] These findings may be compared with the number of rejections for physical reasons of men selected for military service. Proponents of the centers consider that many of the nonmalignant conditions encountered are precancerous, and that prompt attention to them prevents the development of cancer. This viewpoint involves a rather broad concept of precancerous conditions.

Although it is premature to evaluate cancer-detection centers, the experiences should be dispassionately reviewed from the standpoint of expense of operation in relation to cases found at a significantly early stage. Follow-up studies of the cases with negative findings should give information regarding the number of cases overlooked. It may well be found that greater numbers of early cancers can be found with less expense of time and money by intensified education of the laity to report early symptoms and of the medical profession to evaluate these early symptoms.

Diagnosis

Interest in cytologic methods of diagnosis from smears continues unabated,[8–11] although many orthodox pathologists preserve a commendable reluctance to accept the findings without reservation.[12] The application of this technic to permit early evaluation of the efficacy of radiation treatment of carcinoma of the cervix, proposed by Graham,[13] may prove to be valuable in the selection of cases requiring surgical intervention. A series of 280 aspiration and punch biopsies was reported by Ellis,[14] with "useful results" in 63 per cent. Meatheringham and Ackerman[15] reported 300 aspiration biopsies on lymph nodes. In 69 aspirations no lymphoid tissue was obtained. A positive diagnosis of carcinoma was made in 147 specimens, and cancer subsequently developed in 32 cases in which the aspiration specimen was negative. Several authors express a warning against aspiration biopsy in possibly operable lung tumors, because of the danger of pleural implantation. Isaacson and Rapoport[16] reported a series of 34 cancer patients who presented an eosinophil count of more than 10 per cent. It is not generally realized that this degree of eosinophilia may be caused by cancer. In 90 per cent of cases multiple metastases were present.

Lymphatic Spread

There has been considerable interest in recent years in amplifying and confirming knowledge of the pathways of lymphatic spread. The brilliant studies of Gilchrist and David[17] on the lymph-node metastases of carcinoma of the colon and rectum have greatly influenced the concept of the radical operations for dealing with these cancers. Similar methods of study were employed by Coller, Kay and MacIntyre[18, 19] in cancer of the stomach, colon and rectum. Sweet[20, 21] has contributed to knowledge of the lymphatic spread of carcinoma of the esophagus. Warren and Tompkins[22] have drawn attention to the correlation between prognosis and the numerical extent of lymph-node metastases. Whereas it is generally conceded that lymph-node involvement is usually embolic rather than by permeation, it is evident that the concept of permeation frequently influences the plan of operation, and it remains true that removal of the regional lymphatic vessels en bloc along with the primary focus is an ideal cancer operation when it is feasible.

Surgical Treatment

Critical review of autopsy material discloses that in many cases death from cancer is due to the local extension of the disease, with interference with the functions to adjacent normal organs, rather than to widespread metastatic involvement. Realization of this fact, in conjunction with the general lowering of mortality and morbidity after radical surgery, has led to increasingly radical operative procedures to cope with advanced stages of local disease. Although these operations are too recent to permit evaluation of long-term cures, they offer the possi-

bility of cure in many cases hitherto regarded as inoperable, and in most cases find justification at least as effective palliative procedures. While Brunschwig has written extensively on this subject, the tendency is evident in almost all fields of cancer surgery.

Oral Cancer

No single report indicates the trend in the field of oral cancer, but many surgeons are reviving the concept of a one-stage operation for lesions of the tongue, floor of the mouth and cheek, with simultaneous neck dissection and, when necessary, resection of the jaw. These operations can be applied to some cases considered inoperable by conventional standards. Since the procedures are based upon the concept of spread by permeation, which is not the usual method of lymphatic involvement from these cancers, in many cases they show no advantage over the two-stage operations currently practiced. In addition, in coping with inoperable intraoral lesions, they must demonstrate results more satisfactory than those now obtainable by intensive radiation. Although these radical operations undoubtedly have a place, it is likely that their field of employment will be a restricted one.

Cervical-Lymph-Node Metastases

There has been increased willingness on the part of certain surgeons to carry out radical neck dissections bilaterally, with a short interval between the two sides. This procedure involves sacrifice of both internal jugular veins, as well as the anterior and external jugular veins, and is not without danger of causing cerebral damage. In most cases it is probably safer to preserve the internal jugular vein on one side, and it is usually possible to do so. Sugarbaker and Gilford[23] recently drew attention to the combination of neck dissection and jaw resection in cases in which lymph nodes present fixation to the mandible. This procedure has been employed in many clinics, and the dangers of postoperative complications of shock, hemorrhage, sepsis and pneumonia have diminished.

Carcinoma of the Larynx

New et al.[24] have reported the excellent results obtained by radical surgery in carcinoma of the larynx. Whereas it is true that many of the early cases are amenable to radiation therapy, there is agreement that laryngectomy is the procedure of choice in more advanced cases,[25, 26] and there is evidence that subradical surgical procedures are more effective than radiation in most early cases.

The possibility of training patients in esophageal use of the voice makes laryngectomy more acceptable. Brunschwig[27] has carried out very radical laryngectomy for advanced disease, removing regional lymph nodes and any other structures that may be implicated in the spread of the disease.

Carcinoma of the Lung

Most authors recognize the desirability of removing enlarged lymph nodes in the vicinity of the hilus, along with the entire lung, in carcinoma of the lung. In addition surgeons have not hesitated to resect invaded areas of pericardium, parietes or other adherent structures. Although no cures have been obtained by these radical extensions, the operations at least fulfill the desideratum of leaving no obvious disease behind.[28, 29]

There has been increased recognition of the feasibility and desirability of carrying out pulmonary resection for solitary metastasis of sarcomas and carcinomas, and occasionally long-term arrests or even cures are effected.[30]

Carcinoma of the Esophagus

The extent of operations for esophageal carcinoma has increased, with better understanding of the intramural and lymphatic spread of the disease. In this field also Brunschwig and Camp[31] have described a very radical extirpation of the total cervical esophagus. Garlock[32] and Sweet[21] have contributed to elucidation of the technical problems of resections.

Carcinoma of the Stomach

Coller's[18] studies of metastases have emphasized the desirability of more radical operations for carcinoma of the stomach. Longmire[33] and Wahren[34] have advocated total gastrectomy as a better operation for cancer than subtotal gastrectomy. However, the mortality from total gastrectomy still remains relatively high,[35] and the survivors, even those who are cured of cancer, may be significantly impaired in health.[36] All authors emphasize the urgent need for earlier recognition[37] and for a radical approach to the problem of gastric ulcer.[38, 39]

Miscellaneous Abdominal Carcinomas

In the field of multiple and apparently inoperable abdominal carcinomas, Brunschwig[40, 41] has reported a brilliant series of radical improvisations, as well as modifications of operative technic in carcinomas of the pancreas and duodenum.[42] Resections of the liver for primary carcinoma were reported by Hoyne and Kernohan[43] and by Duckett and Montgomery.[44] Rabinovitch et al.[45] described a series of sarcomas of the intestinal tract. Ehrlich and Hunter[46] reviewed the experience of the Army Institute of Pathology in tumors of the gastrointestinal tract.

Carcinoma of the Rectum

The same unwillingness to accept local fixation as a contraindication to radical operation applies to carcinoma of the rectum. Bricker[47] presented a number of cases in which parts of the male genitourinary tract were included in the resection, even to the extent of total removal of the bladder,

prostate and vesicles, with transplantation of the ureters into the proximal portion of the bowel. In the female patients it is not unusual to include the uterus and posterior vaginal wall in the resection.

Carcinoma of the Cervix

There has been a revival of interest in the radical operation for carcinoma of the cervix,[48] based on the lowered mortality and recognition of the inadequacy of radiation in the control of lymph-node metastases. This operation has also been extended to include certain cases with local invasion of the bladder or rectum or both.[41] The successful outcome of such an operation — total cystectomy, total hysterectomy, lymph-node dissection, abdominoperineal resection of the rectum, vulvectomy, vaginectomy and bilateral ureteral transplantation — is eloquent testimony to improved technology in surgery.

Carcinoma of the Breast

Haagensen[49] has returned to the classic Halsted amputation, with wide skin removal, thin skin flaps and routine skin grafts, in the operation for carcinoma of the breast. Most students believe that this elaborate and meticulous operation is not necessary. Differences in results from various clinics are often attributable to differences in the criteria of operability. Ducuing[50] employs a more radical operation than that usually carried out in this country, removing the fascia of the subscapular muscles and the anterior digitations of the serratus magnus muscle and the subclavius muscle, along with the thoracodorsal and long thoracic nerves. Pickrell et al.[51] described technics employed in localized resections of the thoracic wall in dealing with operative-field recurrences.

Sarcoma of the Extremities

Gordon-Taylor and Patey[52] presented a further review of their series of interinnominoabdominal amputations, chiefly performed for sarcoma of the upper portion of the thigh and pelvis. Pack and Ehrlich[53, 54] have also presented a series of radical amputations, in some cases combined with regional-lymph-node dissections, for a variety of advanced malignant conditions. Again on the basis of the theory of lymphatic permeation, Pack et al.[55] stated, "In the lower extremity for primary melanoma of the foot metastatic to inguinal and femoral lymph nodes, we resort to a hip joint disarticulation combined with a retroperitoneal dissection of the iliac and obturator nodes." This procedure appears to be excessively radical unless the authors intended to restrict it to certain cases of advanced disease. Haggart[56] reported a series of radical shoulder-girdle amputations in the treatment of primary malignant tumors of the humerus.

Malignant Lymphoma

Hellwig[57] reported a series of cases of localized malignant lymphoma in which radical surgery was employed, with five-year cures in a significant number of cases.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

BENJAMIN CASTLEMAN, M.D., *Associate Editor*

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CASE 34171

PRESENTATION OF CASE

A thirty-year-old man, a store clerk, entered the hospital with a complaint of pain in the stomach.

Six months prior to entry the patient noted a dull, heavy, nonradiating, epigastric pain, which occurred in the morning and after meals. It was relieved in part by alkalies and warm milk. There was no nausea or vomiting and no tarry stools, and only a rare stool contained bright-red blood. There had been no anorexia or weight loss. About a week before admission a dull, constant, nonradiating pain in the left flank suddenly developed. Two days prior to admission there was a dull, aching pain in the hypogastrium. This was intermittent in character and resembled the epigastric pain.

Physical examination showed a well developed and well nourished man who was moderately distressed because of hypogastric pain. The lungs were clear to percussion and auscultation. The heart was not enlarged, and no murmurs were heard. There was tenderness in the abdomen to deep pressure, localized mainly just to the left of the umbilicus. Pressure on that area also produced pain in the back. There was no rebound tenderness. In addition, there was definite costovertebral-angle tenderness on the left and in the region of the left kidney. The liver and spleen were not palpable. There was thought to be a group of matted lymph nodes at the base of the left jugular vein.

Examination of the blood disclosed a hemoglobin of 13 gm. and a white-cell count of 8200, with 77 per cent neutrophils. The urine was normal. A stool specimen gave a negative guaiac reaction. The total protein was 7.4 gm., the nonprotein nitrogen 27 mg. per 100 cc., the chloride 98 milliequiv. per liter, and the serum amylase 16 units.

On the day of admission a gastrointestinal series revealed a 5-cm. filling defect on the greater curvature in the prepyloric region. No ulceration was observed, and peristalsis did not pass through the area. A smear and gastric washings showed no malignant cells. An intravenous pyelogram performed on the third hospital day was not entirely satisfactory because of gas and fecal material in the overlying bowel, but demonstrated a delayed secretion of the dye on the left, with a moderate degree of hydronephrosis and hydroureter. Two days later a retrograde pyelogram again showed a left hydronephrosis and some degree of obstruction to drainage of the opaque medium. On the sixth hospital day a gastroscopy showed the greater curvature to be distorted by red, edematous rugae. There appeared to be spasm over this area, and no peristalsis was present. There was a superficial ulceration on the lesser curvature, which measured 1 mm. in depth and 1 cm. in diameter. The appearance described extended about halfway up the body of the stomach and then ended rather abruptly. On the eighth hospital day the patient vomited reddish-brown material and had severe, colicky pain in the left flank that persisted.

On the twelfth hospital day an operation was performed.

Differential Diagnosis

Dr. Daniel S. Ellis: It seems to me that it is very clear that this patient had disease involving the stomach and left urinary tract, and I judge that the same disease involved both organs and that it was a malignant process of some kind. I do not know what kind of operation was performed — whether he had a biopsy or whether he was operated on with the idea of attacking the stomach or left urinary tract. Perhaps the x-ray films will help in determining the nature of the lesion in the stomach, and also reveal the location of the obstruction in the left urinary tract.

Dr. Stanley M. Wyman: Examination of the stomach shows the antrum and prepyloric region to be constantly deformed. On the greater curvature there is a constant pressure defect, which elevates the antrum and prepyloric region. The mucosal folds in the lesser and greater curvatures appear unusually thick and prominent. One can see no definite destruction of the mucosa, however. The duodenal loop is not remarkable, but there is deformity of the cap consistent with an old ulcer. The two films from the pyelogram show a slight degree of hydronephrosis on the left with blunting of the minor and major calyxes, and widening of the ureter and pelvis. The ureter is traced to the body of the fourth lumbar vertebra. There is no obstruction to that point, and there are no visible stones to account for the dilatation. A single film taken from the retrograde examination shows more clearly the hydronephrosis, which has a generalized character with some delay in the passage of dye at the ureteropelvic junction. No definite obstruction of the ureter can be seen. The kidney outline cannot be adequately detected. The kidney is not displaced in position, and there is no evidence of a pressure defect on the kidney itself. The lung fields and heart are not remarkable.

Dr. Ellis: Is there any evidence of a soft-tissue mass at the base of the neck?

Dr. Wyman: No; not in this one film.

Dr. Ellis: It seems to me that there is no question that if we can ever interpret symptoms as being typical of certain diseases, this patient had a peptic ulcer or ulceration in the stomach, and the original symptom of a dull, nonradiating epigastric pain occurring postprandially early in the morning and relieved by alkalies and warm milk is that of an ulcerating lesion in the stomach. The pain seemed to change very definitely and became hypogastric and related to the region of the left kidney. As far as I am able to determine there are no other clues.

I suppose that a simple peptic ulcer can be fairly well ruled out on the basis that both the gastroscopist and the radiologist who examined the patient thought that there was an extensive lesion involving the lower part of the stomach in the prepyloric region. Therefore, I believe that this patient had a malignant lesion involving both the stomach and the retroperitoneal lymph nodes and the left ureter, causing hydronephrosis. Such a condition must have been a carcinoma or a lymphoma of some kind. On the law of averages a patient thirty years old ought not to have carcinoma of the stomach, and it is much more likely that he had a lymphoma. The types of lymphomatous disease possibly involving the stomach and the lymph nodes are reticulum-cell sarcoma, lymphosarcoma and, much less likely, Hodgkin's disease. Still another possibility is tuberculosis, of which there seems to be no indication. If this patient's symptoms were first related to the stomach, I think that he had a prepyloric lesion, which was primary in the stomach and metastasized, involving the left urinary tract, causing pressure on the left ureter, with secondary hydronephrosis, and I shall put lymphosarcoma as the first choice. Having had two cases of renal-cell carcinoma before me today, I suppose I am on the spot to say that this is a third case of renal-cell carcinoma, since things usually come in threes. I think that a primary renal tumor with metastases involving the stomach would be less likely than the other way around — that this was a primary carcinoma of the stomach with metastases involving the left urinary tract. I do not believe that this was a scirrhous type of cancer such as one sees in linitis plastica, although it was certainly an infiltrating lesion from the description.

I shall conclude by saying that this man had lymphosarcoma, primary in the stomach, with metastases involving the retroperitoneal lymph nodes and causing partial obstruction and increasing obstruction to the left ureter. And if he really had lymph nodes in the neck I shall interpret them as further evidence of that diagnosis. If he had Hodgkin's disease or leukemia, I would expect to have some clue from the blood smears, but there are none recorded for me to base such a diagnosis on.

Dr. Edward B. Benedict: I do not remember this case, but from the description I do not believe it is correct to say that I saw the prepyloric area and described the region of the antrum. As I read the description given, there was an ulcer on the lesser curvature, probably in the body of the stomach.

Dr. Ellis: It is reported by you and the roentgenologist that no peristalsis was seen in the lower portion of the stomach.

Dr. Benedict: It probably means that I did not see the antrum and pylorus.

Dr. Ellis: From the x-ray studies and the way I read this summary I interpret them to signify involvement of the lower end of the stomach by an infiltrating type of lesion.

Clinical Diagnosis

Lymphoma involving the stomach wall and retroperitoneal tissues?

Dr. Ellis's Diagnoses

Infiltrating malignant tumor of stomach, probably lymphosarcoma, with metastases to retroperitoneal nodes.

Left hydronephrosis secondary to metastatic involvement of left ureter near left renal pelvis.

Anatomical Diagnoses

Mucous carcinoma of stomach, signet-ring type.

Metastases to mesenteric and retroperitoneal lymph nodes.

Obstruction of left ureter from external pressure.

Hydronephrosis, left.

Congenital hypoplasia of kidney, right.

Pathological Discussion

Dr. Tracy B. Mallory: This patient was explored by Dr. Gephart and a large tumor mass found that involved half the stomach, a portion of the omentum and extended down to the region of the left kidney, which appeared to be entirely involved in the same mass. A biopsy of the tumor showed that it certainly was not lymphoma. It was an epithelial tumor with large vacuolated cells, somewhat suggestive of but by no means typical of renal-cell carcinoma; it was so reported.

The patient was transferred to another hospital, where he died a few days later. The post-mortem examination, kindly made available to us by Dr. John J. Larkin, the pathologist, showed a scirrhous signet-ring carcinoma of the pyloric half of the stomach. A shallow ulceration was present on the anterior wall. The tumor had grown through the gastrocolic omentum to involve the colon and had metastasized extensively in the mesenteric and retroperitoneal lymph nodes. A group of these enlarged nodes surrounded the left ureter, obstructing it by pressure and so producing a hydronephrosis. The right kidney was very small, perhaps congenitally hypoplastic, and also showed hydronephrosis. The right ureter was dilated.

CASE 34172

Presentation of Case

A forty-seven-year-old woman entered the hospital complaining of pain in the left leg.

She was well until one year prior to admission, when she developed pains in the neck and back, had a gradual loss of energy, easy fatigability and an increased appetite, and had frequent loose bowel movements associated with an urgent gastrocolic reflex. There was slight exaggeration of all these symptoms in more recent months. Six months before entry she had a barium enema, which was said to have been negative. Two weeks prior to admission the patient had several short chills and ran a slight fever. Five days prior to admission she developed discomfort in the left calf, which persisted until entry. She also had some transient pain in the right leg and during that time ran a temperature of 101°F. Upon entry she was unable to walk because of severe pain in the left calf. She gave no history of hemoptysis, nausea, vomiting or tarry stools.

Physical examination revealed a very obese woman, weighing 230 pounds. There was moderate tenderness in the left leg, extending from the ankle to 8 cm. above the knee. The left calf was swollen from 1 to 2.5 cm. more than the right calf. There was a positive Homans's sign in the left leg, and there were distended veins over the dorsum of the left foot. The rest of the physical examination was essentially negative.

The temperature was 99.5°F., the pulse 95, and the respirations 18. The blood pressure was 145 systolic, 90 diastolic.

Examination of the blood disclosed a hemoglobin of 13 gm. and a white-cell count of 10,700, with 82 per cent neutrophils. The urine was normal. The sedimentation rate was 38 mm. in one hour. The prothrombin time was 24 seconds (control, 17 seconds).

The patient was immediately started on a course of anticoagulant therapy, beginning first with heparin and then changing to dicumarol. A chest film was interpreted as negative for previous pulmonary infarcts. The fever continued, the temperature spiking to 101°F. in the next few days. On the second hospital day a sharp pain developed in the left lower anterior portion of the chest, with radiation to the shoulder. A friction rub developed over this area in the chest. The prothrombin time after anticoagulant therapy was elevated to 50 seconds. The stools showed a ++++ guaiac reaction. On the seventh hospital day the patient again developed severe pain in the right calf and showed a positive Homans's sign on that side. On the ninth day a bilateral superficial femoral-vein ligation was done under local anesthesia. No thrombi were seen in the vessels. A chest film now showed linear shadows of increased density in the left costophrenic angle and possibly a small amount of fluid. The patient was placed on penicillin because of the development of a cough, with the production of a large amount of mucoid white sputum, and also the presence of rales at both lung bases. Four weeks after admission there was an exacerbation of an acute phlebitis in the left leg. The leg was painful and swollen and was about 10 cm. greater in circumference than the right leg at the popliteal space. These symptoms developed under dicumarol, which

was therefore discontinued and heparin instituted. The white-cell count had risen to 23,400, with 88 per cent neutrophils. Another x-ray film of the chest showed that the left costophrenic shadow had become more linear, and there was also a small area of increased density in the posterior portion of the right lower lobe. In the fifth week pain again developed in the anterior portion of the chest, and a slight, but unmistakable, jaundice appeared. The serum albumin was found to be 2.7 gm. per 100 cc., and the alkaline phosphatase was normal. The cephalin-flocculation test was +++. Much bile was present in all the stools, many of which also showed a ++++ guaiac reaction. The van den Bergh test was 2.3 to 3.3 mg. per 100 cc.

An additional history revealed that one month before entry a sharp pain had developed in the right upper quadrant, associated with anorexia, heart burn and a sensation of epigastric pressure. During that period the patient had lost approximately 14 pounds. In the seventh hospital week epigastric tenderness appeared, and a questionable mass was palpable over the area of maximal tenderness, in the left portion of the epigastrium. Bile continued to be present in the urine and the stools. The total protein was 4.2 gm. per 100 cc., and the van den Bergh was 15.5 to 21.2 mg. per 100 cc. The mass in the epigastrium was thought to have enlarged, but because of the marked obesity of the patient it could not be well outlined. Throughout the latter part of the patient's course the legs had become markedly swollen and edematous. She weighed 270 pounds terminally, and the edema had extended well up into the back. On the sixtieth hospital day the patient became restless and hyperexcitable, the respirations slowed, and she died.

Differential Diagnosis

Dr. Reed A. Harwood: May we see the x-ray films?

Dr. Stanley M. Wyman: This is the film taken on admission. It shows no definite evidence of intrinsic pulmonary disease. The right leaf of the diaphragm is higher than the left — higher than one would expect. The heart shadow is not unusual for a patient of this type. The second set of films, taken ten days later, shows the right leaf of the diaphragm even higher. The films were taken in the supine position, however. There is some indefinite density in the left costophrenic angle, and I believe that there is some fluid in the left pleural cavity. In the lateral film there is a suggestion that the right cavity also has a small amount of fluid in the posterior costophrenic sinus. Eight days later the film still shows indefinite linear density in the left costophrenic angle. It has become smaller, however, and there is some linear density in the right middle lung field. It seems to lie in the base of the right upper lobe anteriorly, close to the chest wall. There is a suggestion of an indefinite round shadow posteriorly in one of the costophrenic sinuses — I believe the right. The next examination still shows density in the anterior base of the right upper lobe and the round density in the base probably of the right lower lobe. There is still fluid in the left pleural cavity and possibly in the right. The final film taken one month after this examination shows the right leaf of the diaphragm to have been elevated, considerably more so than on the previous examination. It is the only available film taken at that time. It makes one wonder about something going on beneath the diaphragm.

Dr. Harwood: Would you say that the x-ray films are consistent with small pulmonary infarcts?

Dr. Wyman: They are consistent with multiple infarcts at the base of the right upper lobe and possibly of the left lower lobe.

Dr. Harwood: The mention of jaundice is the first intimation that there was anything else present in this patient besides thrombophlebitis and multiple small pulmonary infarcts.

I do not get a very clear picture of what the illness was like after the appearance of jaundice. Obviously, she must have been very sick. Was that last film taken with a portable machine?

Dr. Wyman: Yes; it is a film taken at the bedside about seven weeks after the initial films.

Dr. Harwood: The patient was probably too sick to have intensive studies such as a gastrointestinal series. There must be something in the record that would give additional information. Perhaps in summarizing the history some of the negative data were not included.

Dr. Myles P. Baker: The alkaline phosphatase was elevated quite significantly at the first determination when she was mildly jaundiced; the figure was 14 or 17 units per 100 cc. The cephalin-flocculation test was not +++ on the first observation; it was either + or ++, and I believe that the thymol-turbidity tests were negative at first. Perhaps that is of some importance. It is true that the patient was too sick for further x-ray studies. During the period of increasing jaundice she was entirely aware of what was going on and doing her best to meet the doctors' requests, taking carbohydrates and so forth, and never presented the picture of a person in severe liver failure.

Dr. Harwood: Was she conscious to the last day?

Dr. Baker: Yes.

Dr. Harwood: This is one of those interesting cases in which the patient comes in for one complaint, and then, under observation, much more serious disease develops from which the patient dies. I tried, for a short while, to connect the complications with the initial complaints and wondered if she could possibly have had thrombophlebitis of the vena cava. I know very little about this condition, but I think that, if she had had a thrombosis of the vena cava that propagated beyond the entrance of the renal veins, she would not have survived such

an insult for more than a few days, so I ruled that out. Then there was the possibility of a thrombosis of the portal vein. The standard textbooks have very little to say about this, but they speak of the classic symptoms of hematemesis, ascites and severe upper abdominal pain — not a word about jaundice. I suppose that it could cause jaundice, but the information we have does not suggest portal thrombosis. For one thing, we do not know whether she had ascites. Perhaps Dr. Baker can give a little help on that. I think the weight gain of 40 pounds is rather sensational in a person who had such a serious disease, and I suspect that she had ascites as well as massive edema.

DR. BAKER: The patient had such marked edema over the back, loin and flank that it seemed as if she must have ascites, but the percussion note was resonant well over into the side of the abdomen, and one would have to say that the physical signs were not those of ascites, although it was suspected and some observers thought that it was present.

DR. HARWOOD: I am going to guess that she had ascites, but usually in portal thrombosis, the ascites develops rapidly, the taps very often are bloody, and the acute disturbance ordinarily leads quickly to death.

We have to admit that this patient had something wrong with the liver. The evidence of that is the low serum protein found in the fifth week of hospitalization, the positive cephalin-flocculation test and the rising serum bilirubin in the absence of obvious biliary obstruction. The question is, What was the matter with the liver? Did she have cirrhosis of the liver? That is one possibility, with polygonal-cell failure as a cause of the increasing jaundice and death. Dr. Baker has said that she did not present the picture of liver failure. One would expect a different type of death, perhaps a much deeper jaundice, and unconsciousness for several days before death. It seems to me that this diagnosis has been excluded.

Could the patient have had a partial obstruction of the common bile duct, as by stone, or a tumor in the region of the ampulla or in the head of the pancreas? Again, I think not, because at no time did she have clay-colored stools. She could not have developed this degree of obstructive jaundice without clay-colored stools. Obstruction of the common duct from any cause thus seems ruled out.

What are the other possibilities? I suppose that metastatic disease is fairly likely. To go back over the record, "she developed pain in the neck and back, had a gradual loss of energy, easy fatigability and an increased appetite, and had frequent loose bowel movements associated with an urgent gastrocolic reflex," which suggest to me the possibility of some lesion of the upper gastrointestinal tract, or possibly a lesion in the pancreas.

The onset of carcinoma of the pancreas is apt to be insidious. The history does not quite fit that picture. Pancreatic carcinoma can metastasize to the liver, and I suppose it is possible for a situation to develop in which the metastases are largely in the left lobe, pressing on some of the larger bile ducts of the left lobe, whereas those of the right lobe, being uninvolved, permit the passage of bile.

One thinks of carcinoma of the stomach. Again, it does not fit the picture of the complaints that this woman had for a year before admission. The only thing that might fit is the one symptom of the presence of blood in the stool. She had it nearly every time the stool was examined. A carcinoma of the stomach or possibly somewhere else in the gastrointestinal tract might be the explanation of blood in the stools, and metastases to the liver might be the explanation of the jaundice. I have ruled out carcinoma of the large bowel because of the negative barium enema.

I should mention one final possibility, or rather, still another possibility, because there can be no "final" possibility in a case like this — that is, carcinoma of the gall bladder, the common duct or the ampulla. In all these cases jaundice is an early symptom, and it is usually complete. I think these diagnoses have been excluded because there was bile in the stools.

I have not mentioned primary carcinoma of the liver. This condition is most often found as a complication of cirrhosis of the liver. There is some evidence that this patient had cirrhosis, and it is possible that a primary tumor of the liver was also present. Such a diagnosis does not explain the blood in the stools, but this finding could be explained either by the elevated prothrombin time or by portal hypertension.

Although I am far from sure what this woman had, I am going to make diagnoses of cirrhosis of the liver, with a primary carcinoma of the liver, mostly involving the left lobe; thrombophlebitis of the veins of the lower extremities, possibly of the iliac veins; and multiple pulmonary emboli. I am

going to add a second choice — a carcinoma of the pancreas with metastases to the liver.

A Physician: What is the possibility of liver abscess? The diaphragm was elevated. Perhaps there was some fluid there.

Dr. Harwood: I meant to ask about the chart, but I am sure that Dr. Baker would have told me if she had had a high temperature.

Dr. Baker: During the period of active phlebitis, the first week, she had a persistent fever, which subsided later.

Dr. Maurice Fremont-Smith: I want to say a few words about this patient, because I was in charge of her health for ten years up to the time of the last illness, including the beginning of it. Looking back, I realize that something happened that we always try to prevent. I cannot see any way now that it could have been prevented. She was a very high-strung woman, who had a tendency to diarrhea. When I first saw her, ten years ago, she had alternating periods of diarrhea and constipation. This continued off and on during the ten years that I took care of her. The diarrhea was affected by the environment. It stopped entirely after any problem that was puzzling her cleared up. Two years before admission to this hospital I did a rectal examination, and a little material being on the end of the glove, I smeared it on a slide, as I always do, and did a guaiac test, which was +++. Two more specimens of stool were examined, and one was faintly positive and the next negative. On the basis of this blood I insisted that she have a proctoscopy and a barium enema. The proctoscopy was done by Dr. Donaldson, who was able to go the full distance of the proctoscope. The mucosa was normal. No injection, ulceration or tumors were seen, except some small hemorrhoids, which were thought sufficiently bulbous and engorged to account for the bleeding. That was approximately a year before entry. Four months later the patient again had a positive guaiac test, and I wrote to her at that time: "The chances, of course, are very great that there is nothing wrong except the hemorrhoids. On the other hand, we dare not make this assumption. You should have a barium enema and proctoscopy and so forth." At that time the hemoglobin was normal. Barium enema, a month later, was, as stated in the record, absolutely normal, the colon filling rapidly without constant defects or diverticula.

Dr. Baker: The picture of this woman's last illness, as far as the jaundice is concerned, was that she was gradually developing extrahepatic obstruction, judging from the laboratory tests. She had had phlebitis in both legs, and we could not really study her adequately. There was a gradual increase in the evidence of liver-cell damage. We wondered at first about the possibility of common-duct stone, recognizing the impossibility of surgery in the presence of the illness unless faced with absolute necessity. The appearance of tenderness in the epigastrium was important. The epigastric mass became more and more obvious, and was not only tender but also the site of persistent pain. Shortly before she died it became obvious that the liver was huge.

Dr. Harwood: In view of the information that Dr. Fremont-Smith has added, may I change my diagnosis?

Dr. Tracy B. Mallory: Certainly.

Dr. Harwood: I shall put carcinoma of the upper gastrointestinal tract — let us say of the stomach with metastases to the liver — as my first choice, and keep carcinoma of the pancreas as my second choice. Hepatoma now seems very unlikely.

Dr. Edward Hamlin, Jr.: The only thing that Dr. Harwood has not dwelt on is the rather extraordinary lack of efficacy of the treatment for phlebitis. The patient had adequate therapy by both anticoagulins and despite that developed more phlebitis. The veins were tied off at a time when neither vein showed thrombosis above the level of ligation. One would ordinarily assume that the phlebitis at least would not jump the gap. Despite adequate therapy with dicumarol, the lesion went on and both iliac veins became thrombosed. That is unusual and of some importance.

Dr. Harwood: Suggesting a metastatic nodule pressing on the vena cava?

Dr. Hamlin: Suggesting some deficiency somewhere.

Clinical Diagnoses

Carcinoma of liver, metastatic, primary source undetermined, probably pancreas.
Iliofemoral phlebothrombosis.
Pulmonary infarcts.

Dr. Harwood's Diagnoses

Carcinoma of stomach.
Metastatic carcinoma of liver.
Thrombophlebitis.
Multiple pulmonary infarctions.

Anatomical Diagnoses

Adenocarcinoma of ascending colon, with metastases to liver.

Thrombophlebitis of both femoral and iliac veins and of inferior vena cava.

Pulmonary emboli, multiple, with pulmonary infarction.

Dependent edema.

Ascites, slight.

Pathological Discussion

Dr. Mallory: Post-mortem examination showed an enormous liver, weighing over 5 kg., completely replaced by metastatic carcinoma. Only very tiny patches of normal liver tissue could be found anywhere within the organ. The primary site of the tumor was in the ascending colon 3 cm. above the ileocecal valve — a region where x-ray examination with a barium enema is ordinarily very accurate.

Both common iliac veins, as Dr. Harwood predicted, were thrombosed, and thrombus also extended up the vena cava, practically to the mouths of the renal veins. The lower portion of the thrombus in the vena cava showed a considerable degree of organization, indicating that it had been present for a considerable time. There was massive edema of both legs and of the sacral and back regions, undoubtedly primarily dependent on thrombosis of the vena cava. The patient was perfectly vulnerable to vena-cava obstruction because she had had a previous hysterectomy, with consequent destruction of both ovarian veins, which are two of the most important sources of collateral circulation for obstruction of the inferior vena cava. She had had multiple pulmonary emboli, and these had produced a series of infarcts in the lung some of which were old and completely scarred, and others in all stages of more recent development down to one quite fresh one that must have occurred only a few days before death.

Dr. Fremont-Smith: Was there any ascites?

Dr. Mallory: There was only 800 cc. of fluid, which would not have been detectable in this particular patient on physical examination. Whether the extreme enlargement of the liver was sufficient to produce functional obstruction of the vena cava and thereby increase the tendency to thrombosis, I cannot answer with certainty.

Dr. F. Dennette Adams: The tumor itself might account for it.

Dr. Mallory: There were no actual tumor nodules that could be seen pressing on or obstructing the vena cava.

Dr. Adams: I meant that the presence of cancer anywhere in the body more or less tends to facilitate thrombosis.

Dr. Fremont-Smith: How large was the tumor in the cecum?

Dr. Mallory: A small annular lesion at the time of autopsy.

Dr. Hamlin: To go back to the phlebitis. Despite the fact that the prothrombin time without therapy was elevated and despite the further elevation produced by anticoagulants she went on to thrombosis. I am not aware of any comment in the literature that the presence of an overwhelming malignant lesion will produce phlebitis, but it is certainly the impression of people like Dr. Allen that such lesions cause phlebitis. The very fact that this rather paradoxical situation took place indicates that an overwhelming malignant tumor was present.

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BRITISH MEDICINE AT THE CROSSROADS

The National Health Service Bill of Great Britain was enacted by Parliament on November 6, 1946, and unless changed by Parliament will become effective on July 5, 1948. It will take British medicine a long mile down the left-hand road — in company with the rest of Britain's institutions.

According to this act the Minster of Health is made responsible for setting up a service that is intended to improve the "physical and mental health of the people of England and Wales, and the prevention, diagnosis, and treatment of illness, and for that purpose to provide or secure the effective provision of services." These services will be rendered free of direct cost to the recipients.

The Ministry of Health is also charged with indirect responsibility for organizing and maintaining "General Medical Services, Health Centers, and all other health services, such as Maternal and Infant Welfare, Home Nursing and Midwifery." All doctors may join the new services; none are required to. Remuneration is settled by regulation and is made up of a "fixed part-salary" and a capitation fee, the latter decreasing as the number of a doctor's patients rises. The sale of practices, long an accepted transaction in Great Britain, is prohibited.

The opponents of the act point out that it means centralization of authority in the office of the Minister of Health (and England has had five Ministers of Health in seven years); intervention of a social worker between doctor and patient; the promise to its beneficiaries of complete medical, dental and nursing services without obvious cost; and the creation of a great lay bureaucracy to administer the program. It means also an estimated cost of at least $1,800,000,000 during 1948 and, inferentially, the ultimate enslavement of all physicians, dentists and nurses into salaried government positions.

A year ago the British Medical Association, as conservative as cold roast beef was once considered to be, held a plebiscite on the act and voted 23,110 against it and 18,972 in favor, with 14,589 members abstaining. On January 31, 1948, a second plebiscite was held that resulted in a vote of 40,814 against the act, or 89.5 per cent of those voting, and 4,735 in favor of it. Another year of socialism, combined with an unfortunately dictatorial attitude on the part of Aneurin Bevan, the present minister of health, has served to crystallize the opinion of British doctors.

It is difficult to know how much of this stiffened resistance is due to an awakened appreciation on the part of the British Medical Association of what the profession stands to lose when the act goes into effect, and how much it may be the result of Mr. Bevan's apparently unco-operative and dictatorial attitude. From the debates that have taken place on the act one is forced to the conclusion that Mr. Bevan's methods have been coercive and his attitude impolitic even to the point where his judgment seems at times to be under the domination of his emotions. Win, lose or draw in this contest, it would seem that the medical profession of Great

Britain is entitled to be under the direction of a minister with a little more ability to see both sides of a question; a little more desire to please those who must render the service.

No profession or group can afford to be reactionary in times like the present. The order is changing, and every nation, to survive, must turn to some degree to the left. The future of British medicine is unpredictable, but so is the future of all British institutions and of Britain herself, nor is America in any large degree immune. What we must hope for, plan for, strive for is to have a guiding hand in the control of our own destinies and to use it not blindly, stupidly or selfishly, but with a regard for all the factors involved.

THE COMMONWEALTH FUND

THE twenty-ninth annual report of the Commonwealth Fund* not only accounts for grants of $1,614,442 during the fiscal year ending September 30, 1947, but also, on the occasion of the retirement of Barry C. Smith as general director, considers in retrospect what the Fund has accomplished during the years of its existence. The record is one deserving the highest praise and one of which all associated with the Fund may justly be proud. A particular tribute to Mr. Smith's role in the organization is contained in a resolution of the Board of Directors: "Without Mr. Smith's diligence and perspective, it is difficult for his fellow Board members to believe that the Fund could ever have developed its present character or achieved the result that it has." A glance at the past and current activities, which were conceived and carried out under Mr. Smith's direction, reveals how closely the Fund has fulfilled the ideal of its founder: "To do something for the welfare of mankind."

The principal methods by which the Commonwealth Fund has accomplished its mission represent a constructive effort for human welfare in the broadest sense rather than for the relief of emergency needs. The activities of the Fund have included work in child welfare and delinquency, psychiatric rehabilitation of veterans and mental health. Attention has also been given to public health as an aspect of health service, the program being directed toward the teaching of preventive medicine and provision of opportunities for post-graduate study by physicians in private practice, with particular emphasis on public-health service suited to the resources and needs of communities with populations of greater than average density and economic status of better than the average. A major contribution has been an endeavor to improve American health through the rural hospital — a crying need in a country in which the best in talent, training and experience tends to concentrate in the large urban centers and the hospitals connected with universities. Another phase of the program has been directed toward support of research and teaching in medical schools, especially the investigation of underlying physiologic problems. The Commonwealth Fund Fellowships for Britons have unquestionably done much to encourage sympathy and understanding between the two great English-speaking nations and have enabled 41 students, technicians and civil servants from the British Commonwealth to pursue studies of various kinds in the United States.

The appropriations during the fiscal year ending September 30, 1947, continued to reflect the Fund's interest in mental health, public health, rural hospitals, medical education and medical research. The grants were awarded to institutions from New England to California, and fellowships were given to 20 students from the British Isles. Nine new books and three revised editions of previously issued studies were published during the year.

The Commonwealth Fund embodies the best in private philanthropy in a free society. Its program works toward the promotion of good will among men while serving to better the lot of the sick and the needy. In an era of wars and rumors of wars this fidelity to a selfless ideal gives cheer to a world sickened with strife but still far afield from the realization of blessed peace.

**The Commonwealth Fund: Twenty-ninth annual report for the year ending September 30, 1947.* 64 pp. New York: Commonwealth Fund, 1948.

PUBLIC HEALTH — A DIAGNOSIS

THE Massachusetts General Court of 1947 established an interim commission, similar to one set up in 1936, to investigate and report on "the coordination of local, state and federal activities in the field of public health" and "the public health laws and

policies of the Commonwealth." On December 3, 1947, a report was made signed by R. H. Lee, G. W. Dean, F. C. Harrington and J. D. Rivest of the General Court and H. D. Chadwick, M.D., C. M. Hilliard and L. J. Smith, M.D. Dr. C. F. Wilinsky served as consultant, and Drs. Carl E. Buck and Robert E. Rothermel, of the American Public Health Association, were technical advisers. Owing to a very short working period and limited budget the commission confined its studies to a few important problems and has asked that it be revived to permit further study. A major set of recommendations involves simplifying the pattern of the Massachusetts Department of Public Health to give the Commissioner a modern working organization.

The local health units of Massachusetts are the subject of other important recommendations. A quotation from the very interesting report of the commission outlines its opinion on local health administration as follows:

> Massachusetts may take pride in the fact that on the record of its vital statistics as relating to infant mortality, maternal mortality, the absence of smallpox from the Commonwealth, the low typhoid fever morbidity, the provision it makes for hospitalizing tuberculosis patients, and many other responsibilities, it compares favorably with other parts of the country. However, the Commission is not satisfied with just doing a good job — it wants to see the best possible public health program continue to evolve in Massachusetts. That it is not accomplishing all that it might is reflected in tables presented in the appendix in Dr. Buck's report which reveals that in the five-year period, 1941–1945, there were 1,583 deaths from what he calls preventable causes and over 70,000 from controllable causes. On the basis that preventable diseases are preventable and that those listed as controllable could be reduced by one half to one third, he estimates that 6,126 lives could be saved annually; representing, if we choose to evaluate lives in terms of $5,000 each, an annual saving of $30,630,000.
>
> The expenditure of a relatively small amount of money for the development of local health departments would, to a large extent, bring about substantial savings of both lives and money. Experiences in Massachusetts and throughout the nation have convinced the Commission that a definite program for the formation of local health departments must be developed, including legislation providing for their formation, their financial support and their establishment at as early a date as practicable.

The commission has not yet recommended the detailed pattern best adapted for development of local health services in the Commonwealth. It has stated, however, that the greatest needs in the formation of local health departments are the following: a sound, state-wide program of education and health information to bring about universal understanding of the need and value of full-time health services; a plan for state financial assistance in the maintenance of full-time local health departments; and an adequate staff of full-time, well trained public-health personnel with good salaries provided to attract such people.

It is essential that these important suggestions lead to definite action. A very specific recommendation is that the Governor immediately appoint a strong committee to begin the proposed program of health education.

The plan for developing full-time local health services for the whole population is, of course, in accord with principles endorsed by the American Medical Association as one deserving the full support of state and local medical societies.

THE GIRLS' TERM

A BILL recently introduced in the New York State Legislature will, if passed, revolutionize and vastly improve the court method of handling cases involving wayward girls, according to a release of the New York Tuberculosis and Health Association. Any attempt at solving this problem, which is acute in all metropolitan areas, will be watched with interest and hope. The proposed bill has the support of many welfare agencies.

The bill has resulted from the obvious need of a specialized court for the girl of sixteen to twenty-one years, as demonstrated by ten years' experience with New York City's Wayward Minor Court for Girls. This experience has led students of the problem to believe that not minor repairs but a thorough overhauling of present laws is necessary.

A new court to be known as The Girls' Term is proposed. The proceedings of this court will be interpreted as civil in character and outside the Code of Criminal Procedure or the Penal Law. The court will have the power to order that action be taken to correct a situation within its purview, but the penalty for noncompliance will be a ruling of contempt rather than prosecution under a penal statute and in a different court.

Under existing law, parents, who often cause the conditions that are responsible for a girl's way-

wardness, must appear as complainants against their daughter. A situation is thus created that contributes to parent-child hostility rather than to an improvement of these relations. Under the new bill action could be taken on a petition by any responsible person, after the court had made a preliminary investigation. Informal hearings could then be held without the formality of placing girls below eighteen years of age under oath.

Present law requires a police officer who observes a girl conducting herself in a wayward manner to obtain a warrant for her arrest. The proposed law would permit her to be placed in protective custody. Most important of all, the new law, if enacted, provides that an "order of disposition" only need be rendered, and the presiding justice is permitted wide discretion in fixing the terms of such an order.

Gradually, we are breaking away from a puritanical concept of criminality. We are learning that justice may be served better by a helping hand upward than a push with the foot downward. Wayward behavior on the part of any of us may be an expression of insecurity; it should not be treated as a sign of viciousness.

OBITUARY

REID HUNT

1870–1948

Reid Hunt, emeritus professor of pharmacology at Harvard Medical School, died on March 7, 1948, after a long illness. He was the last of the great group of medical scientists that established Boston as an international medical center in the first three decades of the twentieth century.

Dr. Hunt was born in Martinsville, Ohio, on April 20, 1870. He received his education there and at Wilmington College and Ohio University, later receiving his baccalaureate degree from Johns Hopkins in 1891. In 1892 he worked with Binz and Nussbaum in Germany; he then returned to Johns Hopkins, where he received his doctorate in physiology in 1896, simultaneously acquiring his degree in medicine from the University of Maryland School of Medicine. From 1896 to 1898 he served as tutor in physiology at Columbia University College of Physicians and Surgeons. The next two years were spent in Egypt on biologic researches. He then returned to Hopkins and began his work in pharmacology under Abel. From 1902 to 1904 he worked in Ehrlich's laboratory in Frankfort. In 1904 he returned to take the position of chief of the Pharmacological Division in the Hygienic Laboratory of the United States Public Health Service. Here he remained until he came to the Harvard Medical School in 1913 as professor of pharmacology, becoming emeritus professor in 1936.

Few scientists have left as many permanent contributions. His work was planned with meticulous care and carried out with superb operative technic. As a result of this careful attention to all phases of the problem he was investigating his papers are conclusive and complete. His first paper on the accelerator nerves of the heart is a classic. He demonstrated the balance between the parasympathetic and sympathetic nerves in this organ and explained the mechanism of the nervous control of the heart beat. His second major contribution was a study of the toxicity of methyl and ethyl alcohols. Undertaken long before the prohibition era these studies were the basis of important medicolegal decisions during that unhappy period. To the other important landmarks in pharmacology and physiology that were attained through his researches may be added his work on arsphenamine in which he devised a practical method for predicting the toxicity of samples of this drug and enabled the Commonwealth to distribute it without fear of the dreaded reactions that were common in earlier samples.

In addition to his primary interest in the science of pharmacology he had ever in mind the application of scientific principles to the use of drugs in the clinic. He steadily insisted that physicians prescribe drugs by their official or semiofficial names in preference to the use of proprietary names. In this campaign he led the Council on Pharmacy and Chemistry of the American Medical Association and did much to co-ordinate its reports in *New and Nonofficial Remedies* with the decennial revisions of the *United States Pharmacopoeia*. He was president of the Pharmacopeial Convention from 1920 to 1930. As a member of the editorial board of the *Journal* he gave freely of his time and sage advice. From his arrival in Boston he was a familiar figure at all the local medical and scientific meetings, and his encyclopedic knowledge of the literature enabled him to contribute much to the success of the discussions that are such a valuable part of such gatherings.

Personally Dr. Hunt was shy and retiring. He was at his best in conversation with individuals and small groups. He had the faculty of thinking through any problem with such thoroughness that when he spoke in council there was nothing left to be said; because of this faculty his advice was widely sought, and he occupied consulting posts of great variety. Through his conversation there ran a vein of humor and kindliness and a complete absence of bitterness, though his scientific standards were uncompromising. He had a delightful sense of the ridiculous; his conversation abounded in anecdotes of the great and near-great. He especially loved to

tell of Ehrlich and his absent-mindedness. Above all he possessed great charm and captivated all who had the privilege of being with him intimately.

Many honors came to Dr. Hunt: membership in learned societies here and abroad, including the National Academy of Sciences, the American Academy of Arts and Sciences, the Association of American Physicians, the Leopold–Carol Akademie, the Deutsche Pharmakologie Gesellschafft, the American Physiological Society and the American Society for Pharmacology and Experimental Therapeutics. Of the last he was the first secretary and the third president. He was chairman of the Northeastern Section of the American Chemical Society and consultant to the Massachusetts Board of Health and to the Chemical Warfare Service of the United States Army. He was a member of the Drug Standardization Committee of the League of Nations and chairman of the Council on Pharmacy and Chemistry of the American Medical Association.

Dr. Hunt's death removes one of the very last of the group of scientists that raised the United States to a position of eminence in the field of physiology. He in common with his colleagues had a broad biological background to bring to the medical sciences. This gave their researches a fundamental quality that transcended the limits of medical practice. In addition to this background Hunt brought to every discussion his encyclopedic knowledge of the literature including not only his own field but also those of general biology, chemistry and even clinical medicine. The memory he leaves in the hearts of those who knew him intimately is sweet, and his scientific contributions will be a lasting monument.

G. P. G.

MASSACHUSETTS MEDICAL SOCIETY

DEATH

Boyd — Melville G. Boyd, M.D., of Dalton, died recently. He was in his fiftieth year.

Dr. Boyd received his degree from Queen's University Faculty of Medicine, Kingston, Ontario, in 1929.

MISCELLANY

VETERANS ADMINISTRATION RESIDENCY TRAINING IN NEUROPSYCHIATRY

A limited number of openings are available for July 1, 1948, appontment to the Veterans Administration residency training program in neuropsychiatry. This program is under the jurisdiction of the deans of the Boston medical schools (Harvard, Tufts and Boston University). Training in this program, which may be from one to three years, is given at: Cushing Veterans Administration Hospital, Framingham, Massachusetts; Bedford Veterans Administration Hospital, Bedford, Massachusetts; The Mental Hygiene Clinic of Boston; Regional Office of Veterans Administration, Boston; Veterans Administration Hospital, West Roxbury, Massachusetts; and Veterans Administration Hospital, White River Junction, Vermont.

Emphasis in the entire program is on psychiatry with dynamic orientation and includes closed-ward, open-ward, outpatient and child psychiatry and neurology.

Further information may be obtained from the Chief Neuropsychiatrist, Veterans Administration Branch Office No. 1, 55 Tremont Street, Boston 8, Massachusetts.

CORRESPONDENCE

A TIMELY WARNING

To the Editor: The trustees of the Tewksbury State Hospital and Infirmary are much disturbed at the number of patients sent to the Hospital who live only twenty-four or forty-eight hours after entrance. We realize fully that it is difficult to evaluate the condition of many patients suffering from a long chronic disease, and also that removal to the hospital may be justifiable because of economic conditions, even though the patient's condition is serious.

We are writing this letter to call the attention of physicians to the General Laws of the Commonwealth, Chapter 122, Sections 16 and 17, which state that no town officer shall remove a sick person to the hospital unless there is reasonable cause to believe that such removal will not injure or endanger his health and in case of doubt shall obtain a certificate of a competent physician that he has examined the patient and that he can be removed without injury to his health.

Recently a decision was handed down by the Massachusetts Supreme Court affirming a judgment of $7000 against a physician for sending to the hospital, some eighty miles by automobile, a patient who died within twenty-four hours.

Last month a patient was sent from a town some twenty miles from Tewksbury and was found dead on arrival.

We hope that physicians sending patients to Tewksbury will in the future be more careful in their examination of such patients.

Robert L. DeNormandie, M.D., *Chairman*
Board of Trustees

Commonwealth of Massachusetts
Department of Public Welfare
Tewksbury State Hospital and Infirmary

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Studies from The Rockefeller Institute for Medical Research. Reprints. Volume 134. 4°, paper, 605 pp. New York: The Rockefeller Institute for Medical Research, 1947. $2.00.

This volume of studies brings together in one volume the contributions of members of the staff of the Rockefeller Institute scattered throughout many periodicals. The period covered is approximately the first half of 1947.

Health Instruction Yearbook 1947. Compiled by Oliver E. Byrd, Ed.D., M.D., professor of health education and director, Department of Hygiene, School of Education, Stanford University. With a foreword by Clair E. Turner, Sc.D., Dr.P.H., National Foundation for Infantile Paralysis. 8°, cloth, 325 pp. Stanford, California: Stanford University Press, 1947. $3.00.

This basic reference serial, now in its fifth year, abstracts the recent literature on public health. For this volume 323 articles were selected from a total of 1672 read by the editor in 95 different periodicals. The material is divided into twenty-one subject fields. A bibliography of the selected articles is appended to the text. An alphabetical list of sources and a good index conclude the volume. The type, printing and paper are excellent. The volume is recommended for all medical and general libraries and should prove valuable to all persons interested in public health.

Congenital Malformations: A study of parental characteristics with special reference to the reproductive process. By Douglas P. Murphy, M.D., assistant professor of obstetrics and gynecology and research associate in the Gynecean Hospital Institute of Gynecologic Research, University of Pennsylvania. Second edition. 8°, cloth, 127 pp., with 65 illustrations. Philadelphia: J. B. Lippincott Company, 1947. $5.00.

This second edition of a monograph first published in 1940 has been expanded by the addition of a second part on the environmental basis of congenital malformations, comprising a study of a series of cases of maternal pelvic irra-

diation and maternal rubella. The first part, from the first edition, discusses the genetic basis in its various aspects. The author concludes from his studies that human congenital defects usually arise from factors present in the male or female germ cells prior to fertilization, and that after fertilization has taken place, they may be produced either by the action of therapeutic amounts of maternal pelvic radium or roentgen irradiation or by a maternal attack of rubella during pregnancy. Likewise, there is no clinical evidence that irradiation of the human egg cell, prior to fertilization, influences the health or development of the resulting infant, and there is only suggestive evidence that an attack of maternal rubella, prior to conception, influences the development of any following offspring. The existing evidence warrants two statements: when a congenital malformation has a genetic basis, there is a greatly increased chance that subsequent brothers or sisters will also be malformed; and when a congenital defect is due to factors that are not genetic in origin, offspring conceived subsequently should be congenitally malformed only with the same frequency as that commonly observed in the population at large. A selected bibliography and index conclude the volume. The publishing is good. This statistical study should be in all reference medical libraries.

A Text-Book of Pathology: An introduction to medicine. By William Boyd, M.D., Dipl. Psych., M.R.C.P. Edin., F.R.C.P. Lond.. LL.D. Sask., M.D. Oslo, F.R.S.C., professor of pathology and bacteriology of the University of Toronto. Fifth edition, thoroughly revised. 8°, cloth, 1049 pp., with 500 illustrations and 30 colored plates. Philadelphia: Lea and Febiger, 1947. $10.00.

This standard textbook has been revised to date, and much new material incorporated in the text. Sections have been added on stasis, botrymycosis, Tsutsugamushi fever, dermatofibroma, sclerosing hemangioma, hypertensive heart disease, cardiac infarction without coronary occlusion, temporal arteritis, mucosal respiratory syndrome, Löffler's pneumonia, giant-cell pneumonia, chronic disseminated tuberculosis, aspergillosis, intestinal lipodystrophy, alloxan diabetes, renal anoxia, malakoplakia of the bladder, interstitial-cell tumor of the testis, primary splenic neutropenia, pyridoxin-deficiency anemia, the anemia of infections, fibrous dysplasia of bone, hyperostosis frontalis interna, ondotogenic tumors, the relation of vitamin C to bone repair and other subjects. The sections on carcinogenesis in relation to enzymes and viruses, silicosis and anthracosis, neurosis and cirrhosis of the liver, Cushing's syndrome, the Rh factor in congenital hemolytic disease, ankylosing spondylitis and Volkmann's contracture have been rewritten. The chapter on allergy, omitted from the previous edition, has been rewritten and restored in this edition. The volume is well published and should be in all medical-reference collections.

NOTICES

ANNOUNCEMENTS

Dr. Charles Isenstein announces the removal of his office to 1587 Massachusetts Avenue, Cambridge, for the practice of ophthalmology.

Dr. David E. Kopans announces the removal of his office to 475 Commonwealth Avenue, Boston, for the practice of obstetrics and gynecology.

Dr. Edward T. Moses announces the removal of his office to 543A Highland Avenue, Malden (48).

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The spring meeting of the New England Obstetrical and Gynecological Society will be held at Hartford, Connecticut, on Wednesday, May 5, with clinics at the Hartford and St. Francis hospitals and a dinner at the Hartford Club.

AMERICAN ORTHOPAEDIC ASSOCIATION

A meeting of the American Orthopaedic Association will be held at the Chateau Frontenac, Quebec, from June 3 to 6. This will be a joint meeting with the British Orthopaedic Association and the newly formed Canadian Orthopaedic Association.

AMERICAN PSYCHIATRIC ASSOCIATION

The 104th annual meeting of the American Psychiatric Association will be held at the Statler Hotel, Washington, D. C., from May 17–20 (the permanent head office of the Association is at 9 Rockefeller Plaza, New York 20, New York), and not in Portland, Oregon, from May 9 to 14, as announced in the April 1 issue of the *Journal*.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, April 29

Friday, April 30

*9:00–10:00 a.m. Medical Experiences in Germany (March, 1948). Dr. Alexander Marble. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

Tuesday, May 4

*12:00 m. X-ray Conference. Margaret Jewett Hall, Mt. Auburn Hospital, Cambridge.

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

Wednesday, May 5

*12:00 m. Grand Rounds and Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*2:00–3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

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*Open to the medical profession.

April 23 and 24. American Society of Anesthesiologists, Inc. Page 582, issue of April 15.

April 26. New England Heart Association. Page 582, issue of April 15.

April 26–29. American Dermatological Association. Page 456, issue of March 25.

April 28. Massachusetts Society for Social Hygiene. Page 582, issue of April 15.

April 29–May 2. American Academy of Pediatrics. Page 240, issue of February 12.

April 30 and May 1. American Gastro-Enterological Association. Page 456, issue of March 25.

May 1. Suffolk District Medical Society. Page 543, issue of April 8.

May 3. American Society for Clinical Investigation. Page 456, issue of March 25.

May 3 and 4. Association of American Physicians. Page 492, issue of April 1.

May 4. Suffolk District Medical Society. Annual Meeting. Page 582, issue of April 15.

May 4 and 5. Association of Military Surgeons of the United States. Page 456, issue of March 25.

May 5. New England Obstetrical and Gynecological Society. Notice above.

May 6. Suffolk Censors' Meeting. Page 344, issue of March 4.

May 6–8. American Association for the Study of Goiter. Page xiii, issue of July 31.

May 11. Harvard Medical Society. Amphitheater of Building D, Harvard Medical School. 8:00 p.m.

May 12–14. American Association of Genito-Urinary Surgeons. Skytop Lodge, Skytop, Pennsylvania.

May 13. Indications for the Use of Forceps. Dr. Roy J. Heffernan, Pentucket Association of Physicians. 8:30 p.m. Haverhill.

May 16–22. American Board of Obstetrics and Gynecology, Inc. Page 344, issue of March 4.

May 16–23. International College of Surgeons. Page 136, issue of January 22.

May 17–19. American Ophthalmological Society. Page 492, issue of April 1.

May 17–20. American Urological Association. Hotel Statler, Boston.

May 17–20. Association for the Study of Internal Secretions. Page 493, issue of April 1.

May 17–20. American Psychiatric Association. Notice above.

May 18–22. American Association on Mental Deficiency. Copley Plaza Hotel, Boston.

May 20–25. American Board of Ophthalmology. Page 170, issue of January 29.

(*Notices concluded on page xv*)